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WOMEN, WORK AND STRESS

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"There is no meaning to life except the meaning man gives his life by the unfolding of his powers." Erich Fromm

ABSTRACT

Work-related stress has become a major public health problem in Western societies. In Sweden women account for the majority of long-term sick leave and the most common reasons are psychiatric conditions such as depression and stress-related diagnoses. Stressful working conditions have been shown to influence both physical and psychological health by acting as important mediating factors in the development of e.g. cardiovascular and musculoskeletal disorders and symptoms of depression and anxiety. However, the majority of stress research has been conducted on men and the results concerning the association between work stress and psychophysiological stress responses in women are still contradictory. Thus, the results cannot automatically be generalized to women as women may experience different stressors, have different perceptions of stress and display different patterns of neuroendocrine reactivity to stress compared to men. Also, midlife has been shown to be a vulnerable phase of life for women entailing both biological and psychosocial changes. Studies of middle-aged women are scarce and there is a compelling need to elucidate the possible association between an adverse psychosocial work environment and stress-related conditions among women of this age group. The overall aim of the present thesis was to study both psychological and physiological effects of stress in middle-aged women focusing on the associations between the effects of adverse psychosocial work environment and physiological stress responses as measured by cortisol as well as lipid levels. A second aim was to study individual differences in a longitudinal perspective by identifying distinct developmental patterns of burnout among the women over a nine-year period.

Study I showed that work-related demands and lack of social support were associated with high cortisol levels. High demands and low social support predicted high cortisol levels at baseline, but not on follow-up. Furthermore, the mean levels of cortisol were lower on follow-up and the women also rated less job strain.

Study II demonstrated an association between the psychosocial work environment and lipid levels as a mediating pathway for women's cardiovascular health at menopause. Job strain predicted an adverse lipid profile, whereas work control predicted a favourable profile. Smoking, BMI and WHR predicted an unfavorable lipid profile. Age was associated with lipid levels at baseline and on follow-up. HRT use was a significant predictor of lower cholesterol levels in the multivariate analyses. Higher socio-economic status predicted positive change in HDL cholesterol whereas lower SES predicted a negative change.

Study III identified distinct subgroups of women showing different developmental patterns of burnout during a nine-year period. Furthermore, the findings showed that the development of burnout was accompanied by concurrent changes in life stress, sleep problems, depression as well as work-related and individual factors.

The results of this thesis offer further empirical evidence for an association between work-related demands and high cortisol levels in women. Also lack of social support was associated with high cortisol levels. The findings provide increased support for an association between an adverse psychosocial work environment and lipid levels as a mediating pathway for women's cardiovascular health at menopause as job strain predicted an unfavourable lipid profile, whereas work control predicted a favourable lipid profile. An important contribution was the identification of different subgroups of women showing different developmental patterns of burnout across a nine-year period,

a result that stands in contrast to previous research suggesting that burnout is a stable construct over time. Moreover, the thesis showed that the development of burnout was accompanied by concurrent changes in life stress, sleep problems, depression as well as work-related and individual factors.

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LIST OF ABBREVIATIONS

ACTH	Adrenocorticotrophic hormone
ANOVA	Analysis of variance
BMI	Body mass index
CAR	Cortisol awakening response
CBI	The Copenhagen Burnout Inventory
CES-D	Center for Epidemiological Studies – Depression scale
CHD	Coronary heart disease
CI	Confidence interval
COR	The Conservation of Resources Theory
CRH	Corticotropin releasing hormone
CVD	Cardio vascular disease
DCM	Demand-Control model
DCM-IV	The Diagnostic and Statistical Manual of Mental Disorders, 4 th Ed.
GAS	The General Adaptation Syndrome
HC	Homogeneity coefficient
HDL	High-density lipoprotein
HPA	Hypothalamic-Pituitary-Adrenocortical
HRT	Hormone replacement therapy
ICD-10	International Classification of Diseases, 10 th revision
LDL	Low-density lipoprotein
NS	Non-significant
OR	Odds ratio
R ²	Explained variance
rANOVA	Repeated-measures analysis of variance

SAM	Sympathetic-Adrenal-Medullary
SD	Standard deviation
SES	Socioeconomic status
SMBQ	Shirom-Melamed Burnout Questionnaire
SOC	Sense of coherence
SPSS	Statistical Package for Social Sciences
SSP	Swedish universities' Scales of Personality
T1	Time 1, First wave of measurement
T2	Time 2, Second wave of measurement
T3	Time 3, Third wave of measurement
MBI	Maslach Burnout Inventory
WHR	Waist-to-hip ratio
β	Beta standardized regression coefficient
η^2	Eta square
χ^2	Chi square

INTRODUCTION

The nature of work has changed profoundly over the past few decades. The positive aspects of these changes include increased individual freedom and flexibility (Hellgren, Sverke, & Näsvall, 2008). On the other hand, work demands and work pace have increased considerably over the last decade leaving many employees experiencing feelings of stress and exhaustion. The recent trends in work life are characterized by technical development, reorganizations, decreased job security and unclear work roles. Consequently, work-related stress has become a major public health issue, with adverse consequences for individual health and quality of life, and with increasing economic challenges for Western countries. In Sweden, these trends are mirrored in the substantial increase in long-term sickness absence in recent years (*Social Insurance Report*, 2010).

In Sweden women are employed to the same extent as men but the nature of women's and men's work is different. We have a segregated labor market in which women and men tend to occupy different positions and where gender equality has not yet been achieved with respect to salaries (*Könssegregering i arbetslivet*, 2001). Furthermore, women continue to carry a major part of responsibility for child care and household duties which may result in greater conflict between work role and domestic life for women than that experienced by men. These contrasts are likely to be among the factors contributing to the fact that women account for the majority of long-term sick leave. It is interesting that nearly one third of the total number of all who were sick-listed in recent years have been women aged 50-59. The most common reasons for long-term sick-leave for Swedish women are psychiatric conditions such as depression and stress-related diagnoses (*Social Insurance Report*, 2010).

Stressful working conditions have been shown to influence both physical and psychological health by acting as important mediating factors in the development of e.g. cardiovascular and musculoskeletal disorders (Bosma et al., 1997); (Hammar, Alfredsson, & Johnson, 1998); (Kuper & Marmot, 2003) and symptoms of depression and anxiety (Williams et al., 1997). High demands at work were found to be related to increased symptoms of poor health among middle-aged women (Muhonen & Torkelson, 2003). A recent study suggests a link between work stress and Type-2 diabetes in middle-aged women (Agardh et al., 2003) Psychosocial stressors may also affect health-related behaviors such as smoking, alcohol consumption, food intake and exercise habits (Steptoe, 1991).

The majority of stress research has been conducted on men and thus the results cannot automatically be generalized to women (Hallman, Perski, Burell, Lisspers, & Setterlind, 2002; Lundberg, 1996). Women differ from men in their experience of symptoms. Several studies have shown that women not only report more symptoms, but that they actually suffer more physically and mentally than men do (Gijsbers van Wijk & Kolk, 1997; E. M. Hall, 1992; Tibblin, Bengtsson, Furunes, & Lapidus, 1990). Women may also experience different stressors, have different perceptions of stress (Hallman, et al., 2002; Lundberg,

Mardberg, & Frankenhaeuser, 1994) and display different patterns of neuroendocrine reactivity to stress compared to men (Collins & Frankenhaeuser, 1978; Kirschbaum, Wust, & Hellhammer, 1992; Schulz, Kirschbaum, Pruessner, & Hellhammer, 1998). In one set of studies women showed lower reactivity to mental stress than men did, however their subjective ratings of emotional reactions to stress were frequently higher than those of men (Collins & Frankenhaeuser, 1978).

It should be pointed out that women have been underrepresented in research on general diseases such as diabetes, infectious diseases and cancer. Despite recent implementation programs to ensure equality of representation for both sexes in clinical studies women continue to be markedly underrepresented in epidemiological and clinical research on coronary heart disease (Maas & Appelman; Schenck-Gustafsson et al., 2011). The reasons for the exclusion of women are not fully understood. There is also a bias in clinical practice in cardiology with respect to medical diagnostics and treatment; women do not receive the same intensive evaluation and treatment or follow-up as men do. Given the relative inattention to women in stress research and clinical research on CHD it is not surprising that data linking stress to health outcomes is also lacking for women in studies of work stress (Eller et al., 2009). Studies of middle-aged women are scarce and there is a compelling need to include women in research in order to elucidate possible associations between negative aspects of the psychosocial work environment and stress-related conditions among women of this age group.

The overall aim of the present thesis was to study both psychological and physiological aspects of stress in middle-aged women. The main focus was on the associations between adverse psychosocial work environment and the physiological stress responses in terms of cortisol and lipid levels. This thesis also analyzed individual differences in a longitudinal perspective by identifying developmental patterns of burnout over a time period of nine years in these women. The data derives from a population-based, longitudinal study of health profiles, lifestyle and ratings of the psychosocial work environment among menopausal women.

BACKGROUND

Theoretical framework

The theoretical framework of this thesis includes the Biopsychosocial Model which entails the study and measurement of physiological and behavioral indicators of stress and relates these to health outcomes. Also, the disciplines of health psychology, psychosomatic medicine and behavioral medicine are relevant to this field of research.

The definition of *Health psychology* states that it is “the aggregate of the specific educational, scientific and professional contributions of the discipline of psychology to the promotion and maintenance of health, the prevention and treatment of illness, the identification of etiologic and diagnostic correlates of health, illness, and related dysfunction, and the improvement of the health-care system and health policy formation” (Matarazzo, 1980).

Another discipline closely related to health psychology is *Psychosomatic medicine* which regards disease to be linked to both biological as well as psychological and social factors. A recent review defines psychosomatic medicine as “comprehensive, interdisciplinary framework for assessment of psychosocial factors affecting individual vulnerability and course and outcome of any type of disease”. The definition also includes “holistic consideration of patient care in clinical practice and integration of psychological therapies in the prevention, treatment and rehabilitation of medical disease” (Fava & Sonino, 2010).

Behavioral medicine is defined as “the interdisciplinary field concerned with the development and integration of behavioral and biomedical science knowledge and techniques relevant to health and illness and the application of this knowledge and these techniques to prevention, diagnosis, treatment and rehabilitation” (Schwartz & Weiss, 1978).

All these fields overlap each other and have similar goals such as prevention, diagnosis, treatment and rehabilitation of illness. The distinction between them regards to what extent they are interdisciplinary: both behavioral medicine and psychosomatic medicine integrate the knowledge and techniques of behavioral science with the medical discipline. Health psychology overlaps these fields as well but is regarded as a specialty within the discipline of psychology (Brannon & Feist, 2007; Lyons & Chamberlain, 2006).

The concept of stress

The foundation of the modern concept of stress is Claude Bernard’s (Bernard, 1961) idea that physical challenges to the integrity of an organism provoke responses to counteract those threats. He based this idea on the notion that the functions of complex living organisms are determined by both the external and the internal environment, and thus, the maintenance of life is dependent on keeping the internal environment constant in the face

of chances occurring in the external environment. This idea was further developed by Walter Cannon (Cannon, 1929) who invented the term *homeostasis* to characterize the processes maintaining this internal stability. Hans Selye was also concerned with severe challenges to homeostasis and the first to use the concept of stress systematically. He defined stress as the sum of nonspecific changes produced by the organism as a way to adapt to severe threats. Selye also introduced the term stressors of agents which cause stress responses.

Selye formulated the general adaptation syndrome (Selye, 1956, 1976) which describes a physiological response pattern to prolonged stressors. The GAS consists of three phases: the alarm reaction, the stage of resistance and the stage of exhaustion. The first stage is the immediate response to a stressor as the body mobilizes itself to meet the threat. This occurs by physiological arousal that includes the activation of the sympathetic nervous system and the release of stress hormones by the endocrine system. In this stage, humans exhibit a "fight or flight" response, which prepares the body for physical activity. During the second phase the body continues to release stress hormones in order to maintain increased arousal and thus adapts to the stressors it is exposed to. However, if the stress persists over a long period of time the body's resources are being depleted and the body will eventually reach a stage of exhaustion which involves increased vulnerability to disease.

A recent textbook on psychology (Passer et al., 2009) defines stress as follows: "A pattern of cognitive appraisals, physiological responses and behavioural tendencies that occur in response to a perceived imbalance between situational demands and the resources needed to cope with them".

The allostasis model

The body's ability to maintain stability through adaptation during stressful situations is called allostasis (Sterling & Eyer, 1988). The bodily response to a challenge is twofold: first, the allostatic response that initiates a complex adaptive pathway is turned on and when the threatening situation has passed, the response is turned off. The process of allostasis is essential to survival as "through allostasis, the autonomic nervous system, the HPA-axis, the cardiovascular, metabolic and the immune systems protect the body by responding to internal and external stress. The price of this accommodation to stress can be allostatic load, which is the wear and tear that results from chronic overactivity or underactivity of allostatic systems"(McEwen, 1998).

According to the allostasis model there are four different situations that may contribute to allostatic load over time. The first type is chronic stress. It is the frequency and intensity of responses that determine how much allostatic load is eventually accumulated. The second type involves lack of adaptation to repeated stressors that are similar and results in prolonged exposure to stress hormones. The third type of response involves an inability to

turn off the allostatic responses. In the fourth type of allostatic load inadequate responses lead to compensatory activation of other systems.

Individual differences

Individuals differ in their responses to stressors both physiologically and behaviourally depending on how a challenge is perceived. These individual differences are a product of genetic predisposition, developmental influences and experience, and result in differential interpretations of experiences. Thus, some individuals are resilient and cope with stress easily while others are more vulnerable. Personality traits act as a filter for external events and thus determine to what degree a threat will be perceived as a stressor (McEwen & Stellar, 1993). Also, a person's general state of physical health determines the individual response to a potentially stressful situation (McEwen, 1998).

Active coping may protect from the negative impact of stressors as individual resources play a relevant role in decreasing vulnerability to stress. Antonovsky (Antonovsky, 1979, 1987b, 1993) proposed a theory called Sense of Coherence (SOC) which focuses on factors that can serve to protect an individual's health. Sense of coherence is an orientation towards life that defines the extent to which an individual perceives the environment as comprehensible, manageable and meaningful. The theory hypothesizes that an individual with a strong SOC maintains his/her health through effective and flexible coping with stressors. SOC has been negatively related to various types of ill health and disease (Kivimäki et al., 2002; Kouvonen et al., 2008; Lindfors, Lundberg, & Lundberg, 2005) and positively related to subjective health (Eriksson & Lindstrom, 2006; Suominen, Helenius, Blomberg, Uutela, & Koskenvuo, 2001). A longitudinal study (Kalimo, Pahkin, Mutanen, & Toppinen-Tanner, 2003) reported that SOC was the most important personal resource that differentiated between employees with and without serious burnout.

Lazarus and Folkman (Lazarus & Folkman, 1984) define coping as “constantly changing cognitive and behavioural efforts to manage specific and/or internal demands that are appraised as taxing or exceeding the resources of the person”. Thus, it is an individual's interpretation of a specific event as threatening or not, as well as of the available resources that are of importance to the experience of stress. According to this model three kinds of appraisals are identified: primary, secondary and reappraisal. Primary appraisal includes an evaluation of an event as stressful, positive or irrelevant. Secondary appraisal involves the evaluation of the available resources as well as different options for coping behaviour. The appraisals can also be re-evaluated and modified by reappraisal. The appraisal process determines not only cognitive and behavioural responses but also physiological responses to a situation. This model classifies coping strategies as problem-focused and emotion-focused. The emotion-focused forms of coping include various cognitive processes that are aimed at reducing emotional distress that a certain situation causes. Problem-focused coping includes a wide array of problem-oriented strategies such as defining the problem, finding alternative solutions and acting upon the best suitable one in terms of costs and

benefits. This type of coping can be directed at changing the situation or the self in means of cognitive changes such as learning new skills or by shifting the level of aspiration.

Work stress: Demand Control Model

The Demand Control model (DCM) developed by Karasek (R. A. Karasek, 1979) and Karasek and Theorell (R. Karasek & Theorell, 1990) is one of the most frequently used models to examine work stress. The model was developed for work environments where stressors are chronic and is based on psychosocial characteristics of work. The model includes two components: psychological demands and decision latitude, which is also called as the control dimension. Work demands refer to psychological stressors at work, e.g. having to work hard and fast and having a high workload. Decision latitude (control) refers to the workers' opportunities to use their skills and to make decisions about their own work. Decision latitude thus includes two components: decision authority and skill discretion. Decision authority refers to the freedom to make one's own decisions concerning one's work (how and what to do) and skill discretion refers to the worker's opportunity to use one's skills and knowledge and the opportunity to learn new things.

The central principle of the DCM model is the assumption that high psychological demands and low decision latitude interact with each other and thus affect learning and personal development and the likelihood of developing psychological strain. Thus, by combining different levels of demands and decision latitude the model predicts four different work experiences: *high strain* (high demands – low decision latitude), *active work* (high demands – high decision latitude), *passive work* (low demands – low decision latitude) and *low strain work* (low demands – high decision latitude).

The model proposes two main hypotheses: the strain hypothesis states that the most detrimental effects on health may result from work situations characterized by high strain, the combination of high demands and low control (job strain). The second hypothesis states that when high demands are combined with high levels of control this active working situation predicts increased motivation, learning opportunities and personal development as outcomes.

The second hypothesis has been less investigated than the strain hypothesis. The active work situation predicts only average psychological strain since the worker experiences the stressors as challenges and thus engages effective problem solving. This work situation is also characterized by high productivity and ability to improve coping strategies which facilitate possibilities to psychological growth and learning (Karasek & Theorell, 2000).

Stress responses: Stress and cortisol

The physiological stress response is mediated by two neuroendocrine systems: the sympathetic adrenal-medullary system (SAM), and the hypothalamic-pituitary-adrenocortical axis (HPA). As a response to a sudden and unexpected event the SAM system activates secretion of epinephrine and norepinephrine which increase heart rate, blood pressure and blood flow. This response to acute stress is adaptive in nature, in other words it helps the individual to cope with the situation. The activation of the HPA axis during a stressful event aims also at adaptation and to maintaining homeostasis but it is vital for supporting normal physiological functioning as well. Thus, the end product of this activation, cortisol, has a wide range of effects in the body: it influences the metabolism of cells, fat distribution, the immune system, the cardiovascular system, and also affective and cognitive processes (Kudielka & Kirschbaum, 2005). Under stress, the hypothalamus produces corticotrophin-releasing hormone (CRT) which provokes the release of adrenocorticotrophic hormone (ACTH) from the pituitary. ACTH in turn stimulates the secretion of glucocorticoids from the adrenal cortex. The main glucocorticoid in humans is cortisol and it can be measured in blood, saliva or in urine, and it is one of the most commonly used biomarkers in stress research (Lovallo & Thomas, 2000).

The first to propose that the assessment of the cortisol increase after awakening (CAR) might represent the adrenocortical activity were Pruessner and colleagues (J. C. Pruessner et al., 1997). Thus the CAR has been established as a useful marker of HPA axis activity by collecting saliva samples during the first hour after awakening (Kudielka & Wust, 2008). When strictly referenced to morning-awakening time, free salivary as well as total plasma cortisol levels show a marked increase during the first hour after waking up. On average, peak values are observed during the first 30-45 minutes.

The stress hormones are protective in the short run but can have damaging effects if they are over-produced. Thus, prolonged overactivation of the stress system has been associated with several negative health outcomes, such as diabetes, hypertension, cancer and cardiovascular disease (Koertge et al., 2002; Lundberg, 2005; McEwen, 1998). However, the results concerning the association between cortisol and job strain are still contradictory. Ohlson, Söderfeldt M., Söderfeldt B., Jones and Theorell (2001) (Ohlson, Soderfeldt, Soderfeldt, Jones, & Theorell, 2001) were unable to show a significant correlation between job strain and cortisol among workers in a mainly female sample employed in human service organizations. This study, however, reported an association between high emotional strain and increased levels of prolactin, a hormone affected by stress (Freeman, Kanyicska, Lerant, & Nagy, 2000). Steptoe, Cropley, Griffith, & Kirschbaum (2000) (Steptoe, Cropley, Griffith, & Kirschbaum, 2000) found that job strain was correlated with elevated cortisol concentrations early in the working day among male and female teachers. Luecken et al. (Luecken et al., 1997) showed that cortisol levels measured during a work day in a sample of women were unrelated to job strain but were greater among those reporting high strain at home due to domestic responsibilities. Perceived stress among male and female teachers was found to correlate with increased cortisol levels during the first hour after awakening (J. Pruessner, Hellhammer, &

Kirschbaum, 1999). A Swedish study (Alderling, Theorell, De la Torre, & Lundberg, 2006) reported that women in both high strain jobs as well as in active (high control and high demands) and in passive jobs (low control and low demands) had elevated cortisol levels. These results are surprising as the analyses were based on a relatively large sample and the potential confounders (depression, medication, BMI, smoking and alcohol consumption) were controlled for in this study.

A recent review of the relationship between psychosocial work environment and cortisol reported that cortisol measured in saliva was positively associated with job stress as well as general life stress (Chida & Steptoe, 2009). Similar results were reported by another recent review on cortisol measured in blood and urine (Hansen, Larsen, Rugulies, Garde, & Knudsen, 2009). Although the results were somewhat inconsistent most of the studies included in this review showed that the overall direction of this association was positive. However, these reviews reported no sex differences. Thus, it can be concluded that the results concerning the association between stress and cortisol are still contradictory and accordingly there is a need for further research on work stress and cortisol levels among women.

Cardiovascular health

Empirical studies on cardiovascular morbidity in the 1980's showed that by including social support at work added to the prediction power of the model. The results of these studies indicated that the combination of high demands and lack of control were particularly important to blue-collar men, whereas lack of control and lack of support was more important for women and white-collar men (Johnson & Hall, 1988). Consequently, these studies contributed to the inclusion of the dimension of social support in the original DCM model and resulted in *iso-strain hypothesis*. This hypothesis states that the most harmful work situation is characterized by high demands, low control and low social support. Social support is also predicted to moderate the negative impact of high strain.

Work-related psychological stress is associated with the development of coronary heart disease and the relationship between adverse psychosocial work characteristics and risk of cardiovascular disease has been well documented in the literature (Belkic, Landsbergis, Schnall, & Baker, 2004; Bosma, Stansfeld, & Marmot, 1998; Landsbergis et al., 2001; Tsutsumi et al., 2003; Westerlund, Theorell, & Alfredsson, 2004). The Whitehall II study, a longitudinal cohort study reported that high work demands predicted incidence of coronary heart disease in both male and female civil servants (Kuper & Marmot, 2003). It should be emphasized that the evidence for women has been less conclusive as two reviews (Belkic, et al., 2004; Kivimaki, Head, et al., 2006) found strong support for an association between exposure to job strain and CVD for men, but not for women. More recently, Low et al. (Low, Thurston, & Matthews, 2010) noted that a growing literature supports the importance of psychosocial factors in the development of CVD among women. The researchers pointed out that a number of the earlier reviews did not evaluate the evidence systematically by gender. Furthermore, it is true that the strength of the

association between certain risk factors and CVD may differ between men and women. This may be due to several factors. Work demands together with other commitments such as family may be more critical for women. Women may be exposed to experiences which are less prominent in men such as conflict between family and professional life.

There is also evidence for an association between low control at work and cardiovascular risk (Bildt, Backstig, & Hjelm, 2006; Bosma, et al., 1997; De Bacquer et al., 2005; Rose et al., 2006). Social support by co-workers is assumed to act as a buffer against health problems associated with high job strain and thus, poor social support has been reported to have detrimental effects on cardiovascular health in several studies (Hammar, et al., 1998; Oxenstierna, Ferrie, Hyde, Westerlund, & Theorell, 2005; Vermeulen & Mustard, 2000). However, these results as well have proved to be more inconsistent for women.

Lipids

Lipids constitute a heterogeneous group of naturally occurring substances such as fats (including triglycerides), sterols (including cholesterol), phospholipids and fat-soluble vitamins (such as A,D,E, K). The biological functions of lipids include energy storage, as structural components of cell membranes, the protection of internal organs, heat conservation and as important signaling molecules. Since the lipids are insoluble in water, they are transported in association with proteins. These lipoprotein complexes include apolipoproteins and enzymes, of which the most commonly known are the high-density lipoproteins (HDL) and the low-density lipoproteins (LDL) (Malloy & Kane, 2001).

There is substantial inter- and intra-individual variability in lipids and lipoproteins. This variation can partly be explained by genetic, biologic (e.g. age and anthropometric variation) as well as by behavioural differences (e.g. diet, smoking, physical activity, alcohol intake) (Lussier-Cacan, Xhignesse, Kessling, Davignon, & Sing, 1999; Niaura, Stoney, & Herbert, 1992). However, as these factors contribute only to a fraction of the variability it has been suggested that also psychological factors may influence the variability between and within individuals. Thus, several studies have reported an association between psychological stress and atherogenic changes in lipid levels that have been unrelated to both diet and physical activity (Doornen, Snieder, & Boomsma, 1998; McCann et al., 1999).

Cardiovascular disease (CVD) is the number one cause of mortality in women in industrialized countries (Landsbergis, et al., 2001). In Sweden it is the underlying cause of 43% of all deaths (*Causes of death 2004*). The known risk factors for CVD for women include elevated total cholesterol or LDL cholesterol, low HDL cholesterol, high blood pressure, diabetes, obesity as well as life style variables such as smoking, and physical inactivity (P. Collins, 2002). Jacobs et al. (Jacobs, Mebane, Bangdiwala, Criqui, & Tyroler, 1990) emphasized that the most important predictive factor for women is a low HDL level. In addition to these risk factors, the Interheart study, a worldwide case-control study across 52 countries identified also abdominal obesity, low fruit and vegetable intake,

and psychosocial factors as accounting for 94% of the risk in women (Yusuf et al., 2004). The psychosocial factors measured in this study were depression, locus of control, perceived stress and life events.

Female sex hormones are thought to play a protective role against heart disease during women's fertile years, whereas women run the same risk as men of developing CVD after menopause (Rosano, Vitale, & Fini, 2006). Several studies have reported that postmenopausal women have higher total cholesterol, LDL cholesterol, triglycerides and lower HDL cholesterol levels than premenopausal women of the same age (Berg et al., 2004; Carr et al., 2000; Fukami, Koike, Hirota, Yoshikawa, & Miyake, 1995; G. Hall, Collins, Csemiczky, & Landgren, 2002; K. A. Matthews, Kuller, Sutton-Tyrrell, & Chang, 2001; Nerbrand, Lidfeldt, Nyberg, Schersten, & Samsioe, 2004). Decrease in HDL was found to be associated with menopause in a longitudinal study of Australian women (Do et al., 2000). A study by Matthews et al. (K. A. Matthews et al., 1989) showed an unfavourable effect of menopause on lipid metabolism, which in turn may contribute to an increased risk of CVD. Also, Kuh et al. (Kuh et al., 2005) found that naturally menopausal and hysterectomized women had higher levels of metabolic risk factors as compared to premenopausal women of the same age. However, contradictory results have also been reported. A review of eighteen observational studies conducted between 1966 and 2004 (Atsma, Bartelink, Grobbee, & van der Schouw, 2006) concluded that there was no convincing evidence that postmenopausal women have an increased risk of developing cardiovascular disease. On the other hand, Schenck-Gustafsson et al. (2011) (Schenck-Gustafsson, et al.) in a more recent review stated that postmenopausal women have an increased risk of CHD.

Menopausal women

The midlife is a period in women's life encompassing a transition that involves not only biological but also psychological and social changes. All women who reach midlife will experience menopause which is defined as the permanent cessation of menstruation. The perimenopausal and early postmenopausal period is characterized by a gradual decline of ovarian activity and fluctuating levels of endogenous estrogen. Declining levels of estrogen are thought to be associated with menopausal symptoms. Hot flushes and night sweats (vasomotor symptoms) are the most common symptoms among women in Western industrialized countries. Other symptoms such as depressed mood and decreased quality of sleep may be related to the presence of vasomotor symptoms (K. Matthews, 1992). However, it should be noted that there are large cultural differences in the experience of vasomotor symptoms (A. Collins, 2002) (Gold et al., 2006).

The biomedical model of menopause has focused on the biological aspects of declining hormonal levels and on identifying climacteric symptoms and thus, according to this model menopause is mainly characterized as a deficiency disease requiring medical treatment, that is hormone replacement therapy (HRT). Research on menopause has

therefore been influenced to have a strong focus on pathology and medical treatments (Olazabal Ulacia et al., 1999).

The psychosocial model, on the other hand, conceives menopause as a normal event that is part of the evolutionary development of women and thus a time for continued growth and development. The experience of varying degrees of ill health during midlife is attributed to personal situations of stress, such as challenges to deal with life events involving e.g. children leaving home, caring for ailing parents, marital problems or possible changes in professional standing or income level (Olazabal Ulacia, et al., 1999). Thus, there is clearly a need for a more holistic model that integrates these two opposing views. One such model is the biopsychosocial model which conceives menopause as a complex, multifaceted process that involves both changes and subsequent adaptations (Olazabal Ulacia, et al., 1999).

The hormonal changes during menopause, particularly the decreased levels of estrogen have an impact on metabolism. The metabolic syndrome encompasses a range of conditions known to be CVD risk factors, such as abdominal obesity, atherogenic dyslipidemia, hypertension and insulin resistance (Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004). The metabolic syndrome is prevalent in both women and men but it is more strongly associated with CVD risk in middle- aged women (Knopp, 2002).

Burnout

Burnout was originally a term used to refer to the effects of chronic drug abuse (Schaufeli & Enzmann, 1998). In a scientific publication it was first used by the American psychiatrist Freudenberg (1974) (Freudenberg, 1974) who had observed how highly committed volunteers who worked with young drug addicts experienced a gradual energy depletion and loss of motivation. Since the 1980's the research literature has been mainly dominated by a multidimensional measure of burnout, called the Maslach Burnout Inventory (MBI). According to Maslach (1997) (Maslach & Leiter, 1997) the definition of burnout is: "burnout is a syndrome of emotional exhaustion, depersonalization and reduced personal accomplishment that can occur among individuals who do 'people work' of some kind". The MBI consists of three dimensions: Emotional exhaustion, depersonalization and Personal Accomplishment. Emotional exhaustion refers to the experience of being depleted of physical energy and of emotional resources. Depersonalization is characterized by feelings of detachment and the development of cynical and uncaring attitudes towards one's clients or care recipients. Reduced personal accomplishment is viewed as increasing feelings of inadequacy and reduced efficacy (Maslach, 1993; Maslach & Leiter, 1997).

The MBI reflects the belief that burnout is a problem restricted to persons working within the human service professions and thus it was developed for use in human services, health care and education (Maslach & Jackson, 1981). This view was however changed as an adapted version of the MBI for general occupations was later developed (Maslach,

Jackson, & Leiter, 1996). However, Maslach never expanded burnout to apply outside the domain of work (Maslach, Schaufeli, & Leiter, 2001). The MBI has been criticized to some extent as the factorial validity has been found to be “poor”(Bakker, Demerouti, & Schaufeli, 2003) .

Even though the MBI has strongly influenced the conceptualization of burnout, there are several other theoretical approaches and instruments that are used to investigate burnout.

The Copenhagen Burnout Inventory (CBI), developed by Kristensen, Borritz, Villadsen and Chistensen (2005) (Kristensen, Borritz, Villadsen, & Christensen, 2005) consists of three separate scales for assessing burnout in different domains: personal burnout, work-related burnout and client-related burnout. The CBI has been shown to have satisfactory reliability and validity.

Hallsten (2005) (Hallsten, Josephson, & Torgén, 2005) has proposed a model that describes burnout as a process that may occur in any context that is conceived as important to one’s self-esteem. According to this model, burnout is defined as follows: “Burnout is assumed to occur after unsuccessful self-esteem strivings, activated and maintained by enduring or recurring stressors in central life domains and roles.” The process leading to burnout is divided into three phases. The first phase that is called “Anxious engagement” is characterized by high involvement and engagement, worry and anxiety. If the coping efforts during the second phase do not lead to reaching the desired goals, a phase of frustration may follow. Eventually, additional experiences of striving and defeat, may in turn lead to the phase of burnout. Thus, performance-based self-esteem is regarded as a psychological construct or orientation that may be activated by enduring environmental demands. It can be regarded as a vulnerability factor for high psychic strain and distress which originates from performance standards that are aimed at gaining both self-esteem and social approval. The self-esteem striving perspective on burnout is measured with a scale for Performance-based self esteem (Pbse-scale) (Hallsten, et al., 2005).

Another multidimensional definition of burnout was developed by Shirom and Melamed. They conceptualize burnout as “the depletion of an individual’s energetic resources – a combination of physical fatigue, emotional exhaustion and cognitive weariness” (Shirom, 1989). This definition implies a long-term exposure to emotional demands and can be applied to both occupational settings and to those outside work situation. It also takes life conditions into account. The definition is based on the Conservation of Resources Theory (COR) which stipulates that individuals are highly motivated to obtain and protect their resources (Hobfoll, 1989). The Shirom-Melamed Burnout Questionnaire (SMBQ) (Kushnir & Melamed, 1992) assesses the dimensions of physical fatigue (lack of energy and tiredness), emotional exhaustion (lack of energy to invest in relationships with colleagues), and cognitive weariness (slow thinking and low mental alertness) (Melamed, Shirom, Toker, Berliner, & Shapira, 2006).

Despite the disparities among the theoretical approaches to burnout, one dimension may be recognized as the core experience in burnout as persistent fatigue or exhaustion seems

to receive most support in longitudinal research (Melamed, et al., 2006). As disturbed sleep was found to be an important predictor of fatigue (Akerstedt et al., 2004) it is not surprising that an association between sleep problems and burnout has been reported by earlier research using both self-reports (Grossi, Perski, Evengard, Blomkvist, & Orth-Gomer, 2003; Melamed, et al., 2006; Peterson et al., 2008; Tokuda et al., 2009) and physiological measurements (Ekstedt et al., 2006; Soderstrom, Ekstedt, Akerstedt, Nilsson, & Axelsson, 2004).

The researchers have still not reached a consensus on the definition of the concept of burnout. One of the questions still debated is whether burnout is primarily work related or whether it can develop in non-occupational settings as well. Thus, since the dominance of the MBI and its restriction to work-related burnout there is a lack of instruments that can be applied to settings outside work. There is also a lack of descriptive and explorative studies, as well as longitudinal and qualitative approaches on burnout.

Burnout does not exist as a formal diagnostic label in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) issued by the American Psychiatric Association (2000). In the International Classification of Diseases (ICD-10) issued by the World Health Organization (WHO, 1992) burnout is included as a diagnosis under the category "Problems related to life-management difficulty" (code Z73.0) and includes the diagnosis of vital exhaustion. According to ICD-10 burnout can also be diagnosed as neurasthenia (code F48.0) which includes symptoms of increased fatigue, difficulties to concentrate, exhaustion, muscular pains, dizziness, headaches, irritability, sleep disturbances and minor degrees of both depression and anxiety.

In Sweden burnout was introduced as a diagnostic label in 1997 when it for the first time was included in the Swedish translation of the ICD-10 (Friberg, 2006). The ICD-10 is integrated with the Swedish social security system as the various classifications of diseases are used to qualify a person for economic compensation. In 2005, the diagnostic label "Exhaustion-syndrome" was added in the national version of the ICD-10 (*Ändringar i och tillägg till Klassifikation av sjukdomar och hälsoproblem 1997 (KSH97) - systematisk förteckning*, 2005). The criteria for this syndrome are: physiological or mental symptoms of exhaustion during at least two weeks, and obvious/essential lack of mental energy. Furthermore, at least four of the following symptoms must have been present almost every day during a two-week period: difficulties to concentrate, decreased ability to cope with stress, emotional lability or irritability, sleep disturbances, physical weakness, physical symptoms like chest pain, palpitations, and dizziness. The symptoms must cause significant clinical suffering or deteriorated functioning at work, socially or in other important occasions. Additionally, the symptoms must not be related to other psychiatric or medical diagnosis or substance abuse. Whether the criteria for depression or anxiety are present at the same time, the diagnosis of exhaustion-syndrome will be regarded as a secondary diagnosis.

A recent review presents evidence for an association between burnout and detrimental effects on physical health, such as an increased risk of cardiovascular disease, metabolic syndrome, dysregulation of the HPA-axis, systemic inflammation, impaired immunity functions and poor health behaviors (Melamed, et al., 2006 Berliner, & Shapira, 2006). In addition, sleep disturbances, depression and anxiety have been linked to burnout (Grossi, et al., 2003; Peterson, et al., 2008). It is estimated that about 4-10 % of the working population suffers from severe burnout in the Nordic countries and the Netherlands and this prevalence can be regarded as indicative of the situation in most other industrialized countries (Kristensen, et al., 2005; Schaufeli & Enzmann, 1998; Shirom, 2005).

AIMS OF THE THESIS

The overall aim of the present thesis was to study both psychological and physiological aspects of stress in middle-aged women. The main focus was on the associations between adverse psychosocial work environment and the physiological responses to stress in terms of cortisol and lipid levels. This thesis also investigated developmental patterns of burnout over a time period of nine years in these women.

The specific aims of the empirical studies:

Study I

The aim of the first study was to investigate whether there is an association between serum cortisol and work-related stress, as defined by the demand control-model in a longitudinal design.

Study II

The aim of the second study was to characterize lipid levels of perimenopausal women and to assess whether these are related to psychosocial work environment and work stress as measured by the demand-control model and to life style factors in a longitudinal design.

Study III

The third study had two aims: first, to identify developmental patterns of burnout in middle-aged women from the working population. The second aim was to evaluate whether work-related and individual factors are associated with concurrent changes in burnout.

METHOD

Sample

The present thesis is based on a longitudinal study on menopausal women. The overall aim of the study was to investigate associations between health and the psychosocial work environment and to relate these to the psychological and biological changes that occur during the menopausal years in women's lives.

The study included a baseline, conducted in 2000-01, and two follow-ups, conducted in 2002-03 and 2007-09. A two-phase sampling procedure was used. In the first phase a random sample of 2000 women aged 49-53 residing in Stockholm and its suburbs was drawn from the Swedish Population Register by consulting a demographic expert. In order for the sample to represent the socioeconomic status of urban middle-aged women, a random sample was drawn based on their yearly income level (low 20%, medium 60%, and high 20%, respectively, from each group). The cohort received an invitation letter to participate in the study together with a questionnaire on socioeconomic background, health and lifestyle.

In the second phase a random representative sample of 200 women was drawn from the pool of 940 women who had completed the questionnaire. The final percentage in the income groups at baseline was as follows: low 6.7%, medium 61% and high 32%. The group of 200 women received a second invitation and gave their written consent to participate in the study. 162 women participated in the baseline, 142 had complete data. 136 women had complete data in the first follow-up and 118 women in the second follow-up. Two of the women were deceased between the first and the second follow-up. The general outline of the study is described in table 1.

Table 1. General outline of the study

	<u>Year</u>	<u>Age</u>	<u>n</u>
Baseline	2000-01	49-54	142
1 st follow-up	2002-03	51-56	136
2 nd follow-up	2007-09	56-62	118

Procedure

The procedure used throughout the study included both psychological and biological measures and covered blood sampling, anthropometric measures, a psychological interview and the completion of a questionnaire.

The women received the questionnaire during the interview, responded to it at home and mailed it to the researchers in a prepaid envelope. Up to three reminders were mailed to those who had not responded in two weeks time. In addition, women who did not reply despite of the written reminders were called personally. In order to avoid missing values, the women who had missed to fill in some questions received copies of these pages in the questionnaire and returned them by mailing them.

Interview

The semi-structured interviews were conducted face-to-face at the Psychology Department at the Karolinska Institute by trained interviewers and lasted 1-1½ hours. The interviews covered the following areas: sociodemographic background, health and lifestyle (e.g. regular physical activity, smoking and alcohol use), social relationships, leisure time, and the experience of the psychosocial work environment (e.g. demands, stress at work, work satisfaction, and social support).

Blood samples

Blood samples were drawn between 8:00 and 9:00 a.m. after an overnight fast at the Department of Otorhinolaryngology at the Karolinska University Hospital. The samples were analyzed in the laboratory of Clinical Chemistry at the Karolinska University Hospital.

Anthropometric measures

Measurements of blood pressure, weight, height, waist and hip were performed before the interview at the Division of Psychology at the Karolinska Institute. Blood pressure was measured with an automated blood pressure device (Dinamap Monitor 1846) after 5 minutes of resting sitting. Body weight was measured using an electric scale (Tanita BWB-800). Waist measurements were obtained using a non-stretch tape at the narrowest part of the midsection, while the hip was measured at its widest part. Waist-to-hip ratio (WHR) was calculated by dividing the waist circumference by the hip circumference (Rebuffe-Scrive et al., 1987). The measurement of height was based on self-report. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Assessments

Stress

Work stress

Work demands, control and social support at work were measured according to the Demand-control model by Karasek and Theorell (R. Karasek & Theorell, 1990). Indices (calculated as means) were constructed using items from the Job Content Questionnaire (R. Karasek, Baker, Marxer, Ahlbom, & Theorell, 1981) and from the Total Workload Questionnaire (Mårdberg, Lunberg, & Frankenhaeuser, 1991). The index for *work demands* consisted of four items, e.g. "Do you have enough time to do your work tasks?". The index for *work control* consisted of seven items, e.g. "To what extent can you influence the content of your work?". The items were scored on a seven-point frequency scale, ranging from 1 (*not at all*) to 7 (*to a high degree*).

Studies I and II: Social support was based on two questions from the interview, "Do you have support from your co-workers in your work?" and "Do you have support from your supervisor in your work?". Answers were coded as "yes/no, partly/ have no co-workers/supervisor. *Yes* and *partly* were assigned the value 1 and *no* and *have none* the value 0. The mean was then calculated for this index.

Study III: The index for *Social support* consisted of six items that were included in the questionnaire on the second follow-up, e.g. "To what extent do you receive support from your supervisor?".

Jobstrain was calculated by dividing the score for work demands by the score for work control.

Study I: Stress at work was measured using a question included in the interview, "Do you experience stress at work?". The answers were coded as yes/no. A follow-up question was "What kind of stress do you experience?". The answers were read and reread by the research team and the following categories were formed based on the women's responses: time pressure, attending to several things at the same time, not being able to influence work, too great responsibility/ too high demands, conflicts at work, poor leadership, and lack of staff/lack of resources.

Life stress was constructed as a variable that combines both domestic stress and work stress. It was assessed using two questions from the questionnaire: "Are you affected by contradictory demands either in your domestic life or at work?" and "Do you experience stress in your current life?". The answers were coded as *yes*=1 and *no*=0 and *yes*- answers were followed up by a question that was rated from 1 (*very little*) to 7 (*very much*). The individual was assigned the value 1 if either of the questions was rated as ≥ 5 .

Biomedical measures

Cortisol was measured in blood and analyzed with time-resolved fluoroimmunoassay kits (Perkin Elmer, Finland) in the Laboratory of Clinical Chemistry at the Karolinska University Hospital.

Lipids and lipoproteins

Blood samples were drawn after an overnight fast (8-9 am), frozen immediately and stored at -70°C. High density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol and triglycerides were analyzed in the laboratory of Clinical Chemistry at the Karolinska University Hospital. Cholesterol and triglyceride levels were determined using enzymatic methods and HDL using homogenous methods (with automatic analyzers LX20, Beckman Coulter; Modular P, Roche Diagnostics). LDL was calculated using the Friedewald equation (Friedewald, Levy, & Fredrickson, 1972). Total cholesterol/ HDL and LDL/HDL ratios were calculated, since they have been shown to be powerful tools for predicting CHD (Shai et al., 2004).

Lifestyle

Smoking was assessed using questions in the health questionnaire. The women were classified as either current smokers or non-smokers (past or never smokers).

Alcohol consumption was assessed using the following questions in the health questionnaire: “How often do you drink alcohol?”, “What kind of alcohol do you usually drink?”, “How much alcohol do you usually drink during one week?”. An average weekly intake of alcohol was calculated and converted into grams of alcohol. One centiliter (cl) of pure alcohol equals to 7.89 grams (g) of alcohol. Three categories of groups were defined according to a report from the National Institute of Public Health (*Alcohol and health*, 2005): no alcohol intake (0g alcohol/week), low to moderate intake (1-108g/week) and high intake (>108g/week).

Fat consumption was measured using a validated dietary questionnaire “20 questions on your dietary habits” (Lingfors et al., 1994). It has been used since 1989 separately or together with other questionnaires as a part of characterizing health profiles. The questionnaire includes items on daily dietary habits, e.g. the amount and type of fat used and type of dairy and meat products consumed.

Physical activity was assessed using the question: “Do you participate regularly in a physical activity that makes you sweat or feel out of breath?”. Answers were coded as *yes* and *no*. Accordingly, the women were categorized as physically active or inactive.

Individual factors

Sense of coherence was measured using the 13-item scale rated 1 (*never*) - 7 (*always*) by Antonovsky (1987) (Antonovsky, 1987a). An overall SOC score was calculated as a mean of all items with high scores indicating a strong SOC.

Personality was assessed with the Swedish universities Scales of Personality (Hallman, et al.) at baseline (Gustavsson et al., 2000). It consists of 13 subscales out of which two were chosen to be used in this study: Psychic trait anxiety (PTA) and Stress susceptibility (SS) as these subscales were significantly associated with burnout in preliminary analyses (PTA: $F=62.6, p<0.001$; SS: $F=36.2, p<0.001$).

Medical conditions

Sleep problems were measured using three items from the Menopause Symptom Inventory (Sarrel, Rousseau, Mazure, & Glazer, 1990 & Glazer, 1990): “I have difficulties falling asleep”, “I wake up too early” and “I wake up at night sweating”. The items were scored on a seven-point frequency scale, ranging from 1 (*never*) to 7 (*always*). An overall sleep difficulties index (mean) was calculated for each of the participants.

Depression was assessed with the Center for Epidemiologic Studies – Depression Scale (CES-D) (Radloff, 1977). The scale consists of 20 items scored on a four-point frequency scale, ranging from 1 (*not at all*) to 4 (*always*). An overall depression score was calculated as a sum for each of the participants.

Burnout was assessed using the Shirom-Melamed Burnout Questionnaire (Melamed, Kushnir, & Shirom, 1992 1992; Melamed et al.; Shirom, Westman, Shamai, & Carel, 1997 & Carel, 1997) containing 19 items rated 1 (*never*) to 7 (*always*). The SMBQ focuses on an overall mental and physical exhaustion in life by measuring different aspects of burnout: burnout, tension, listlessness and cognitive difficulties. An overall burnout index (mean) was calculated for each participant. The burnout index was dichotomized into low (1.0-3.9) and high burnout (4.0-7.0) based on cut-off values received in clinical practice and previous studies (Grossi, et al., 2003; Norlund et al., 2010; Soares, Grossi, & Sundin, 2007)

Hormonal status

Menopausal status was assessed from the responses to questions concerning menstrual changes during the previous 12 months and during the previous 24 months on follow-up. Criteria by Avis & McKinley (Avis & McKinlay, 1991) were used to define the menopausal status. Premenopausal status was defined as regular bleeding, perimenopausal status as irregular bleeding or changes in the bleeding pattern during the preceding 12 months and postmenopausal status as absence of menstrual bleeding for at least 12 months. Women who had undergone surgical menopause were excluded from the analyses ($n=2$).

HRT use. The women were classified as current HRT users if they had been on hormone replacement therapy (HRT) for a minimum of 2 months previously, otherwise as non-users.

Statistical analysis

Study I

Associations between cortisol and the work environment were studied using the indices of demands, control and social support. Univariate analyses included Pearson's correlations and analyses of variance. The Post hoc comparisons were carried out using the Scheffe test. Comparisons between the baseline and the follow-up were carried out using paired T-tests. Multiple stepwise regression analyses were performed in order to investigate the relationship between work stress and cortisol. Logistic regression analyses (Tabachnick & Fidell, 2001) were used to identify variables that significantly contributed to high and low cortisol groups. For the purpose of logistic regression analyses the data was divided into three groups: low, medium and high levels following consultation with our endocrinological expert, Professor Britt-Marie Landgren. Based on long-standing clinical experience the groups were defined as follows: the low level group 180-350 nmol/l, medium level group 351-449 nmol/l and high level group 450-900 nmol/l. All the statistical analyses were carried out using the SPSS version 13.1 (SPSS Inc., Chicago, Illinois, USA).

Study II

Associations between the lipids and the psychosocial work environment were studied using the indices of demands, control and social support. Univariate analyses included Pearson's correlations, chi-square tests, and analyses of variance. The Post hoc comparisons were carried out using the Scheffe test. Comparisons between the baseline and the follow-up in lifestyle variables and lipid values were carried out with paired *t*-tests. Distributions for triglycerides were skewed and were therefore log transformed prior to analyses. Mahalanobis distance was counted in order to detect multivariate outliers, but none were found. Multiple stepwise regression analyses were performed in order to investigate the relationship between psychosocial job stressors, life style and the lipid levels. Significance criterion for entry of the variables was $p \leq 0.05$ and for removal $p \leq 0.1$. No variables were forced in the models. All statistical tests were two tailed and *p*-values less than 0.05 were considered significant. SPSS version 14.0 (SPSS Inc., Chicago, Illinois, USA) was used to run all the analyses.

Study III

As the aim of the study was to identify and classify individuals with similar burnout trajectories, a cluster analysis was performed using SLEIPNER 2.1 (Bergman & El-Khoury, 2002). Initially the RESIDUE module of SLEIPNER was used to scan the dataset for potential outliers that might distort the clustering process. Four women were identified as outliers and were removed from the dataset. The cluster analysis was performed using a sample including 116 women.

Ward's hierarchical method was used when performing the cluster analysis. This method was chosen since it has been shown to recover true cluster-belonging and to consistently

replicate clustering (Breckenridge, 2000). Based on the recommendations of Bergman, Magnusson and El-Khoury (2003; L. R. Bergman, D. Magnusson, & B. M. El-Khoury, 2003), three criteria were used to assess satisfactory fit of the cluster solution. Firstly, the explained error sums of square (EESS) of the cluster solution should not be lower than .67. Secondly, the homogeneity coefficient for respective cluster should be lower than 1.0. Thirdly, the merging of two clusters should be reasonable and make theoretical sense.

Since the clustering method used was hierarchical, this could result in that some individuals ended up in clusters where they did not optimally belong. This would consequently have a negative effect on the overall fit of the cluster solution, impairing both the EESS and the homogeneity coefficients of the clusters. The RELOCATE module of SLEIPNER was therefore used to reposition individuals so they ended up in a cluster where they were fitted better. Finally, the centroids of the cluster solution were used to perform a K-means cluster analysis on the original sample (including the four individuals identified as outliers). SPSS 18.0.3 was used to perform the K-means cluster analysis.

Mean values and standard deviations of burnout over time were then computed for each cluster. The rank-order stability of burnout levels over time was calculated as Pearson test-retest correlations. A univariate repeated-measures ANOVA (rANOVA) was conducted to assess within-group changes in burnout levels across time for the entire sample. A two-way rANOVA was then performed in order to test if the clusters represented different burnout trajectories. Post-hoc tests were performed to examine the within-subject changes over time for each of the clusters. In order to further validate the cluster solution it was investigated whether changes in burnout for each cluster were associated with concurrent changes in theoretically relevant variables. The variables chosen were job strain, depression, and sleep problems (Ahola et al., 2005; Ekstedt, et al., 2006; Grossi, et al., 2003). A two-way rANOVA was performed to test whether the different developmental patterns of burnout were reflected in concomitant changes in the explanatory variables. For each cluster post-hoc tests were then performed to test for significant changes over time in the explanatory variables. η^2 was calculated as effect size indices. In order to be able illustrate the concurrent development of burnout, jobstrain, depression and sleep problems, Z-scores were calculated. The z-scores were calibrated against the first wave of measurement. For descriptive purposes additional explanatory variables were used to characterize the different clusters: social support, personality subscales “Psychic trait anxiety” and “Stress susceptibility”, sense of coherence (SOC) and life stress. χ^2 -analyses were used to test if the clusters differed regarding these variables at the different waves of measurement. For these analyses the variables were dichotomized as follows: Social support was dichotomized using the mean. Personality subscales were dichotomized using the T-score=50 as this also reflects the population mean. SOC was dichotomized using the median split. The analyses were conducted using SPSS 18.0.3 (SPSS Inc., Chicago, Illinois, USA).

Ethical issues

Ethical approval for the studies was obtained from the regional ethical review board in Stockholm (Dnr 98-315, 00-091, 2007/969-32). The participants were informed about the objectives and the procedure of the studies. They were also informed that the participation in the study was voluntary and about their right to terminate the participation at any time.

The social security numbers of the participants that were received from Swedish Population Register were used to identify the women's current addresses at each time point of data collection. In order to secure confidentiality during the data entry the participants were assigned coded identification numbers. The data are stored in a locked file cabinet which only the researchers have access to.

RESULTS

Table 2. Socio-demographic characteristics of the study participants

Characteristics	T1 (n=142)		T2 (n=136)		T3 (n=118)	
	n	%	n	%	n	%
Marital status						
Married/cohabiting	89	62.7	85	62.5	79	66.9
Single	31	21.8	28	20.6	24	20.3
Widowed	2	1.4	1	0.7	1	0.8
Divorced/separated	20	14.1	22	16.2	14	11.9
Education						
Elementary/primary	6	4.2				
High school/secondary	43	30.3				
University	71	50.0				
Vocational training	22	15.5				
Occupation						
Management	16	11.3	19	14.0	14	11.9
Self-employed	8	5.6	8	5.9	5	4.2
Professional	69	48.6	51	37.5	45	38.1
Administration/service	46	32.4	51	37.5	38	32.2
Employment						
Full time (≤ 35 h/week)	120	84.5	103	75.6	84	71.2
Sick-listed	3	2.1	2	1.5	6	5.1
Unemployed	0	0	2	1.5	5	4.2
Retired	0	0	0	0	4	3.4
Other	4	2.8	3	2.2	0	0
Menopausal status						
Premenopausal	47	33.1	4	2.9		
Perimenopausal	31	21.8	48	35.3	2	1.7
Postmenopausal	21	14.8	46	33.8	105	89.0
HRT use	43	30.3	38	27.9	11	9.3

T1=time 1; T2= time 2; T3= time 3; HRT= Hormone replacement therapy

Table 2 presents the sociodemographic characteristics of the participants throughout the study. A majority of the women were married or cohabiting while one fifth was single. Nearly 50% of the women held academic professional occupations at baseline, and almost 40% at T2 and T3. Approximately 30% of the women worked in the service sector or in administrative jobs.

STUDY I

Cortisol levels

There was a significant difference in cortisol levels between the baseline and the follow-up ($t=2.29$, $p=0.024$). The cortisol levels were significantly lower in the follow-up compared with the baseline.

The effects of menopausal status and the use of HRT on cortisol levels were controlled for by using ANOVAS. At baseline there were no significant differences in cortisol levels between the premenopausal, perimenopausal, postmenopausal groups and the group using HRT ($F=2.00$, $p=0.118$). However, when the women were dichotomized into HRT users and non-users and these groups were compared with each other, there was a significant difference in cortisol between these two groups ($F=5.596$, $p=0.02$). The HRT users had higher cortisol levels than the non-users. On follow-up the groups of premenopause and perimenopause were analyzed together because there were too few women in the premenopausal group. The results showed that there was a significant trend: HRT users had higher cortisol levels than the other groups ($F=2.67$, $p=0.07$). However, when the women were dichotomized to HRT users and non-users and these groups were compared with each other, there was no significant difference in cortisol between the two groups ($F=2.646$, $p=0.107$).

Work related stress

There was a significant difference in job strain (measured as the ratio between demands and control) between the studies ($t=3.45$, $p=0.001$). The women had higher job strain scores at the baseline compared with the follow-up.

Also, when stress at work was measured using a question from the interview ("Do you experience stress at work?") 87.5% of the women in the baseline were stressed compared with 73.6% of the women in the follow-up.

A follow-up question to experience of stress at work was "*What kind of stress do you experience?*". Figure 1 describes the reasons for work related stress measured using the question above. One third of the women in the baseline and at follow-up stated that time pressure is the most significant stressor in their job. 16.7% of the women in baseline experience that they have too great a responsibility or too high demands compared with 6.4% of the women in the follow-up. Other reasons for work related stress were "attending to several things at the same time" (12% of the women in the baseline and 12.8% in the follow-up) and not being able to influence one's work (7.5% in the baseline and 3.2% in the follow-up).

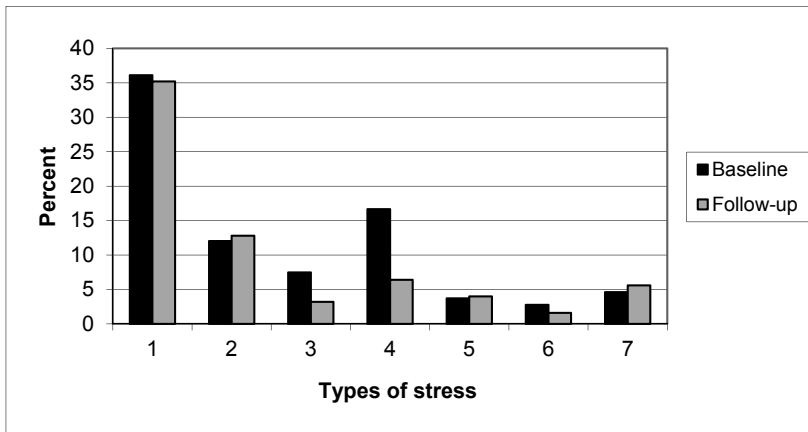


Figure. 1. Types of stress reported by women who experience stress: (1) time pressure; (2) attending to several things at the same time; (3) not being able to influence work; (4) too great responsibility/too high demands; (5) conflicts at work; (6) poor leadership; (7) lack of staff/resources.

Multivariate analyses

Stepwise multiple regression analyses were performed with cortisol as the dependent variable. Two models were created: Model 1 included the indices for demands, control and social support, BMI, WHR and HRT use (coded as a dichotomous variable) as the predictor variables and in Model 2 job strain was included instead of the indices. Table 3 presents the results of the regression analysis. At baseline cortisol levels were significantly predicted by lack of social support ($p<0.05$) and the use of HRT was nearly significant ($p=0.08$). In Model 2 none of the predictor variables was significant (results not shown). On follow-up WHR ($p=0.007$) and HRT use ($p=0.02$) were significant predictors of cortisol in both Model 1 and Model 2. Both WHR and HRT use had an inverse relationship with cortisol.

Table 3. Stepwise multiple regression analyses

Predictors	Baseline		Follow-up	
	β	p	β	p
<i>Model 1</i>				
Demands	0.14	.17	-0.04	.70
Control	0.14	.20	-0.04	.64
Social support	-0.20	.047	-0.05	.61
BMI	-0.11	.26	-0.10	.37
WHR	-0.13	.20	-0.25	.007
HRT use	0.17	.08	-0.21	.02

We were also interested in predicting high and low cortisol levels and therefore performed logistic regression analyses using the indices for demands, control and social support, BMI, and HRT use as predictor variables. The high cortisol group was compared with the low plus medium level groups (as described in the Methods). The results of the logistic regression analysis can be seen in Table 4. At baseline in Model 1 high cortisol levels were significantly predicted by work demands (OR, 1.82; 95% CI, 1.13-2.93; $p < .05$). In Model 2 none of the predictor variables was significant (results not shown). On follow-up none of the predictors was significant in either Model 1 or in Model 2 (results not shown).

Table 4. Odds ratios (OR) of predictor variables for high-cortisol and low-cortisol groups using logistic regression analyses

Predictors	Baseline			Follow-up		
	OR	95% CI	p	OR	95% CI	p
<i>Model 1</i>						
Demands	1.82	1.13-2.93	.01	0.83	0.61-1.14	.25
Control	1.40	0.85-2.29	.19	1.03	0.65-1.62	.90
Social support	0.36	0.06-2.30	.28	1.25	0.29-5.47	.77
BMI	0.98	0.87-1.11	.76	0.91	0.81-1.03	.13
HRT use	1.41	0.54-3.67	.48	2.09	0.85-5.12	.11

STUDY II

Lipid levels

There were no significant differences between the mean levels of the lipids between the baseline and the follow-up (Table 6). However, more than half of the women had high LDL cholesterol levels both at baseline (53.3%) and on the follow-up (57.9%). 63.6% of the women had also high total cholesterol levels at baseline and 65.4% on the follow-up (Table 5).

Table 5. Lifestyle and lipid values of the study participants

<i>Lifestyle</i>	Baseline		Follow-up	
	n	%	n	%
Smoker	30	28.0	21	19.6
Physically active	46	42.9	55	51.4
Overweight BMI 25-30	24	22.4	21	19.6
Obese BMI >30	9	8.4	10	9.3
Hypertension >140/90 mmHg	4	3.7	7	6.5
Use of lipid-lowering drugs	1	0.9	1	0.9
<i>Lipid values</i>				
Low HDL < 1,0 mmol/l	1	0.9	3	2.8
High LDL >3,0 mmol/l	57	53.3	62	57.9
Hypercholesterolemia >5,0 mmol/l	68	63.6	70	65.4
High triglycerides >2,0 mmol/l	5	4.7	5	4.7

Work stress

There was a significant difference in job strain between the two sessions ($t=3.45$, $p=0.001$). The women reported higher job strain scores at the baseline compared with the follow-up. There was also a significant difference in work demands between the sessions ($t= 6.67$, $p< 0.00$). The women experienced higher demands at the baseline as compared with the follow-up (Table 6).

Lifestyle

BMI: 22.4% of the women were overweight (BMI 25-30) at baseline and 19.6% on follow-up. 8.4% of the women were obese (BMI >30) at baseline and 9.3% on follow-up. There were significant differences in lipid levels between women with normal weight, overweight and obese women at baseline: obese women had lower HDL levels (1.42 mmol/l) compared with normal weight (1.84 mmol/l) and with overweight women (1.59 mmol/l; $F=8.1$, $p=0.001$). They also had higher LDL/HDL ratio (2.43 mmol/l comp to 1.7 mmol/l and to 2.3 mmol/l; $F=11.7$, $p<0.00$), and higher total cholesterol/HDL ratio (4.06 mmol/l comp to 3.05 mmol/l and to 3.81 mmol/l; $F=8.3$, $p<0.00$). Overweight (3.49 mmol/l) and obese women (3.37 mmol/l) had significantly higher LDL levels compared with normal weight women (2.98 mmol/l; $F=5.2$, $p=0.007$).

Table 6. Means and standard deviations (SD) of lipid levels and work- related variables

Variables	Baseline		Follow-up		<i>t</i> -value	<i>p</i> -value
	Mean	SD	Mean	SD		
<i>Lipid levels</i>						
HDL (mmol/l)	1.74	0.39	1.74	0.42	0.00	1.00
LDL (mmol/l)	3.09	0.76	3.19	0.75	1.82	0.072
Total cholesterol (mmol/l)	5.33	0.80	5.42	0.83	1.52	0.131
Triglycerides (mmol/l)	1.14	0.73	1.09	0.61	0.56	0.58
LDL/HDL ratio (mmol/l)	1.86	0.66	1.94	0.69	1.74	0.085
Total cholesterol/HDL ratio (mmol/l)	3.19	0.80	3.29	0.95	1.76	0.082
<i>Work related</i>						
Job strain	0.94	0.38	0.81	0.39	3.45	0.001
Work demands	4.58	1.03	3.84	1.44	6.67	0.001
Work control	5.17	0.99	5.02	1.00	1.06	0.29

On follow-up obese women had significantly higher systolic (145.4 mmHg; $F=7.02$, $p=0.001$) and diastolic blood pressure (86.1 mmHg; $F=7.23$, $p=0.001$) than overweight (135.1/75.9 mmHg) and normal weight women (128.4/71.4 mmHg). Obese women also had significantly lower HDL levels (1.41 mmol/l; $F=6.95$, $p=0.001$) than overweight (1.56 mmol/l) and normal weight women (1.8 mmol/l). Obese (3.89 mmol/l) and overweight women (3.9 mmol/l) had higher total cholesterol/HDL ratio than normal weight women (3.06 mmol/l; $F=9.6$, $p<0.00$). They also had higher LDL/HDL ratio (2.34 mmol/l and 2.28 mmol/l; $F=5.2$, $p=0.007$) and higher triglycerides levels (1.41 mmol/l and 1.37 mmol/l; $F=7.39$, $p=0.001$) than normal weight women (1.82 mmol/l and 0.94 mmol/l).

Smoking: 26.7% of the women were smokers at baseline and 17.6% on follow-up. The smokers had following mean lipid levels: HDL 1.7 mmol/l, LDL 3.4 mmol/l, total cholesterol 5.6 mmol/l, triglycerides 1.3 mmol/l, LDL/HDL ratio 2.1 mmol/l, total cholesterol/HDL ratio 3.5 mmol/l at baseline, and following mean lipid levels on follow-up: HDL 1.7 mmol/l, LDL 2.98 mmol/l, total cholesterol 5.2 mmol/l, LDL/HDL ratio 1.96 mmol/l, total cholesterol/HDL ratio 3.6 mmol/l.

Smokers had significantly higher LDL levels than non-smokers (3.4 mmol/l comp to 2.99 mmol/l; $F=5.05$, $p=0.027$), total cholesterol levels (5.6 mmol/l comp to 5.2 mmol/l; $F=6.27$, $p=0.014$), triglyceride levels (1.3 mmol/l comp to 0.99 mmol/l; $F=9.01$, $p=0.003$), LDL/HDL ratio (2.1 mmol/l comp to 1.79 mmol/l; $F=5.63$, $p=0.019$), and significantly higher total cholesterol/HDL ratio (3.5 mmol/l comp to 3.06 mmol/l; $F=7.74$, $p=0.006$) at baseline.

Smokers also had significantly higher total cholesterol levels (5.79 mmol/l comp to 5.3 mmol/l; $F=5.38$, $p=0.02$), triglycerides levels (1.4 mmol/l comp to 0.98 mmol/l; $F=11.16$, $p=0.001$), and total cholesterol/HDL ratio (3.66 mmol/l comp to 3.2 mmol/l; $F=3.97$, $p=0.049$) on follow-up. There were no differences between smokers and non-smokers in

BMI, WHR, alcohol consumption, fat consumption or physical activity either at baseline or on follow-up.

Physical activity: 42.9% of the women were active at baseline and 51.4% on follow-up. There were no significant differences in lipid levels between these groups either at baseline or on follow-up. There were no significant differences on follow-up.

Alcohol: At baseline the mean consumption was 55.1 g/week and 62.1 g/week on follow-up. The women consumed significantly more alcohol during the follow-up ($t=2.28$, $p=0.025$). Women with null consumption were excluded from these analyses. At baseline 2.8% of the women were abstainers, on follow-up 1.9%. The majority of women were moderate drinkers: 88.8% at baseline and 83.2% on follow-up. 8.4% of the women had high alcohol consumption at baseline and 15.0% on follow-up. Women with a high alcohol consumption had significantly higher HDL levels (2.1 mmol/l) compared with the non-drinkers (1.8 mmol/l) and with the low-to-moderate drinkers (1.7 mmol/l; $F=5.18$, $p=0.007$) at baseline. Women with a high alcohol consumption also had significantly lower LDL/HDL ratio (1.29 mmol/l) compared with the non-drinkers (2.24 mmol/l) and with the low-to-moderate drinkers (1.94 mmol/l; $F=4.25$, $p=0.017$).

There were no significant differences in BMI, WHR, smoking or physical activity between these three groups. On follow-up no significant differences in lipid levels between the different groups of alcohol intake were observed, nor were there any significant differences in BMI, WHR, smoking or exercise between these groups.

Socioeconomic status (SES): Occupational status was dichotomized into two groups including managers, self-employed and professionals comprising one group and women in service sector, care, trade and unskilled jobs comprising the second group. Comparison of the two groups showed that women with higher socioeconomic status had better LDL/HDL ratio (1.79 mmol/l comp to 2.08 mmol/l; $F=4.46$, $p=0.037$) and better total cholesterol/HDL ratio (3.07 mmol/l comp to 3.43 mmol/l; $F=5.47$, $p=0.021$). They also consumed less fat ($F=5.87$, $p=0.017$) and had lower systolic blood pressure ($F=9.23$, $p=0.003$) than women with lower SES status at baseline. Women with higher SES also rated having more control over their work situation ($F=23.86$, $p<0.00$) and less job strain ($F=6.95$, $p=0.01$). As for intake of alcohol, BMI, WHR, smoking and physical activity there were no differences between the two occupational groups. On follow-up women with higher SES had significantly lower triglycerides ($F=5.41$, $p=0.022$). They also reported having more control over their work situation ($F=14.48$, $p<0.00$).

Menopausal status and the use of HRT: At baseline 33.6% of the women were premenopausal, 24.3% were perimenopausal and 14% were postmenopausal. Thirty women (28%) were HRT users at baseline. The different menopausal groups and HRT users were compared with each other regarding lipid levels.

There were no significant differences between these groups. However, comparing HRT users with the non-users, HRT users had lower cholesterol levels than non-users, this difference being close to significance ($p=0.057$).

The use of alcohol, BMI, WHR, systolic and diastolic blood pressure, exercise, smoking and fat scores did not differ between the menopausal groups and the HRT users. Furthermore, no differences were found between the users and non-users of HRT.

On follow-up 2.8% of the women were premenopausal, 40.2% were perimenopausal and 31.8 were postmenopausal. Premenopausal and perimenopausal women were pooled into one group since there were too few women in the premenopausal group. This group was compared with the postmenopausal women and with the users of HRT. There were no significant differences in lipid levels between any of these groups. In addition, no differences were found between the users and non-users of HRT.

The use of alcohol, BMI, WHR, systolic and diastolic blood pressure, exercise, smoking and fat scores did not differ between the menopausal groups and the HRT users. There were no differences between the users and the non-users of HRT regarding the variables above.

Women who were pre- or perimenopausal at baseline and had become postmenopausal by the time of the follow-up session ($n=11$), were studied using paired t -tests regarding lipid levels, alcohol use, blood pressure, fat intake and smoking during the two sessions. The postmenopausal women had significantly higher total cholesterol levels compared with their baseline values ($t=2.52$, $p=0.03$). They also had higher BMI ($t=-2.48$, $p=0.032$). No other significant differences between the two sessions were found.

Multivariate analyses

Multiple stepwise regression analyses were performed with HDL, LDL, total cholesterol, triglycerides, total cholesterol/HDL and LDL/HDL ratios as the dependent variables. In order to test both job strain and its individual components as predictor variables, two models were created: Model 1 included the following predictors: the indices for demands, control, and social support, age, HRT use (coded as a dichotomous variable), BMI, WHR, smoking (coded as a dichotomous variable), alcohol consumption, systolic and diastolic blood pressure, and occupation (coded as a dichotomous variable). In Model 2 job strain was entered as a predictor variable instead of the indices of demands and control.

The results of the regression analyses are presented in tables 7 and 8. Control at work was a significant predictor of higher HDL ($p<0.05$), lower LDL/HDL ratio ($p<0.01$) and lower total cholesterol/HDL ratio ($p<0.01$) on follow-up. Job strain predicted higher LDL/HDL ratio ($p<0.01$) and higher total cholesterol/HDL ratio ($p<0.05$). Life style variables smoking, BMI and WHR predicted an adverse lipid profile, whereas alcohol consumption predicted a favourable lipid profile. In order to study the longitudinal effect, changes in lipid levels between the baseline and follow-up were calculated and an additional regression model was created. These change scores were used as dependent variables to predict changes in lipids and the same predictor variables as in the previous models were used. Socioeconomic status (SES) was a significant predictor of change in HDL both in model 1 and 2 ($p<0.05$). The change score for women with a higher SES showed a significant positive change in HDL levels between baseline and follow-up, for women with a lower SES the change was negative ($F=4.97$, $p=0.028$).

Table 7. Standardized β -coefficients of the stepwise multiple regression analyses at baseline

Model 1	HDL	LDL	TCHOL/HDL	Triglycerides †	TCHOL/HDL	CHOL/HDL
Demands	0.201*	0.047	0.112	-0.137	-0.1	-0.122
Control	0.143	0.024	0.158	0.132	-0.013	0.009
Social support	0.115	-0.038	0.013	0.104	-0.019	0.001
Socioeconomic status	0.141	-0.013	0.019	-0.117	-0.037	-0.062
Age	0.144	0.216*	0.258**	-0.026	-0.041	0.015
Smoking	-0.15	0.277**	0.294**	0.301**	0.235**	0.274**
Alcohol consumption	0.363**	-0.254	-0.036	-0.019	-0.334**	-0.316**
HRT use	-0.097	-0.157	0.220*	-0.056	0.017	0.009
BMI	-0.201	0.071	0.025	0.057	0.102	0.099
WHR	-0.233*	0.139	0.04	0.248*	0.274**	0.284**
Systolic BP	-0.036	0.292**	0.251**	0.244*	0.277**	0.294**
Diastolic BP	-0.064	-0.055	-0.059	-0.087	-0.059	-0.074
<i>Adjusted R Square</i>	0.288	0.206	0.203	0.241	0.336	0.366
Model 2						
Job strain	0.038	0.017	-0.024	-0.164	-0.05	-0.072
Social support	0.049	-0.038	0.013	0.104	-0.019	0.001
Socioeconomic status	0.14	-0.013	0.019	-0.117	-0.037	-0.062
Age	0.09	0.216*	0.258**	-0.026	0.041	0.015
Smoking	-0.151	0.277**	0.294**	0.301**	0.235**	0.274**
Alcohol consumption	0.334**	-0.254**	-0.036	-0.019	-0.334**	-0.316**
HRT use	-0.104	-0.157	-0.22*	-0.056	0.017	0.009
BMI	-0.203	0.071	0.025	0.057	0.102	0.099
WHR	-0.223*	0.139	0.04	0.248*	0.274**	0.284**
Systolic BP	-0.047	0.292**	0.251**	0.244*	0.277**	0.294**
Diastolic BP	-0.039	-0.055	-0.059	-0.087	-0.059	-0.074
<i>Adjusted R Square</i>	0.255	0.206	0.203	0.241	0.336	0.366

Table 8. Standardized β -coefficients of the stepwise multiple regression analyses on follow-up

Model 1	HDL	LDL	Total chol.	Triglycerides †	LDL/HDL	TCHOL/HDL
Demands			0.039	-0.061	0.085	0.087
Control	0.210*		-0.118	0.019	-0.275**	-0.247**
Social support	-0.038		0.021	-0.012	0.082	0.052
Socioeconomic status	-0.095		-0.094	-0.036	0.083	0.054
Age	0.115		0.217*	-0.03	0.024	0.037
Smoking	-0.083	NS	0.223*	0.258**	0.151	0.235**
Alcohol consumption	0.195*		-0.189	0.029	-0.235*	-0.258**
HRT use	-0.021		-0.062	-0.034	-0.032	0.02
BMI	-0.272**		-0.003	0.069	0.075	0.12
WHR	-0.174		0.099	0.298**	0.232*	0.278**
Systolic BP	0.027		0.094	0.099	0.078	0.168
Diastolic BP	0.129		0.158	0.036	0.019	0.059
<i>Adjusted R Square</i>	0.179		0.079	0.146	0.193	0.256
Model 2						
Job strain	-0.126		0.106	-0.063	0.244**	0.21*
Social support	0.002		0.021	-0.012	0.094	0.064
Socioeconomic status	-0.023		-0.094	-0.036	-0.003	-0.027
Age	0.123		0.217*	0.03	0.038	0.03
Smoking	-0.066	NS	0.223*	0.258*	0.125	0.214*
Alcohol consumption	0.219*		-0.189	0.029	-0.284**	-0.3**
HRT use	-0.029		-0.062	-0.034	-0.026	0.023
BMI	-0.318**		-0.003	0.069	0.111	0.15
WHR	-0.173		0.099	0.298**	0.283**	0.324**
Systolic BP	0.066		0.094	0.099	0.085	0.171
Diastolic BP	0.162		0.158	0.036	0.022	0.059
<i>Adjusted R Square</i>	0.146		0.079	0.146	0.178	0.24

** $p < 0.01$, * $p < 0.05$; † log-transformed; TCHOL/HDL = total cholesterol/HDL ratio; NS=non-significant

STUDY III

At baseline and on the first follow-up 19.5 % of the women had high levels of burnout, on the second follow-up the prevalence of burnout had declined to 12.9 %. The stability of burnout levels over time was calculated as Pearson correlations and the coefficients were as follows: between baseline (T1) and the first follow-up (T2): $r = 0.72$; between baseline and the second follow-up (T3): $r = 0.49$; and between the first and the second follow-up: $r = 0.52$. There was no overall effect of time on burnout ($F = 1.83$; $p = 0.167$).

Table 9. Means, standard deviations (SD) and Cronbach's alpha coefficients of the studied variables

Variables	T1	Mean (SD)		Cronbach's α		
		T2	T3	T1	T2	T3
Burnout	3.0 (1.1)	3.0 (1.1)	2.8 (1.1)	0.78	0.75	0.77
Job strain	1.6 (0.65)	0.8 (0.41)	0.93 (0.45)			
Social support			5.3 (1.26)			0.91
Sleep problems	2.6 (1.35)	2.9 (1.49)	3.0 (1.51)	0.64	0.69	0.69
Depression	12.5 (0.87)	13.7 (10.3)	12.4 (10.2)	0.77	0.92	0.92
Life stress	5.55 (0.86)	5.71 (0.82)	5.69 (0.84)	0.63	0.52	0.66
Sense of coherence		5.3 (0.77)	5.4 (0.78)		0.81	0.82
Psychic trait anxiety	50.4 (9.9)			0.82		
Stress susceptibility	50.0 (9.7)			0.75		

T1=time 1; T2=time 2; T3= time 3

The cluster analyses resulted in 6 trajectories which explained 75% of all individual variation. Homogeneity coefficients for the clusters ranged between 0.29 and 1.02. A five-cluster solution (merging cluster 1 and 2) also met the recommendations for satisfactory fit. However, this solution was rejected as the two clusters displayed diverging patterns and the difference in magnitude of the levels at T1 was greater than one standard deviation. The mean levels for the cluster solution are presented in Table 10.

The results of the repeated-measures ANOVAs showed that there was a significant interaction effect (cluster \times time) ($F = 22.6$; $\eta^2 = 0.51$; $p < 0.001$) indicating that the clusters represent different trajectories. Also, this interaction effect was significant between T1 and T2 ($F = 12.59$; $\eta^2 = 0.36$; $p < 0.001$) and between T2 and T3 ($F = 33.27$; $\eta^2 = 0.6$; $p < 0.001$). The post-hoc tests revealed that each of the six clusters reflected significant changes over the three waves of measurement. Furthermore, clusters 1 and 2 changed significantly between T1 and T2, and clusters 2,3,4,5, 6 between T2 and T3. The results of the rANOVAs are presented in Table 11.

A description of the clusters

The mean levels for the clusters are presented in Table 10 and graphically plotted in Figure 2 and 3. Statistical tests of changes in concurrent levels of job strain, sleep problems, and depression are given in Table 11. Table 12 shows the χ^2 - tests used in order to characterize the clusters. Social support did not differentiate between the clusters.

Table 10. Mean values (centroids), standard deviations and homogeneity coefficients of the six clusters

Cluster	N (%)	T1	T2	T3	HC
		Mean (SD)	Mean (SD)	Mean (SD)	
1	19 (16.4)	3.68 (0.54)	2.93 (0.42)	2.82 (0.51)	0.48
2	15 (12.9)	2.64 (0.36)	3.7 (0.58)	2.47 (0.38)	1.02
3	17 (14.7)	3.72 (0.88)	3.88 (0.85)	4.8 (0.91)	0.64
4	15 (12.9)	4.11 (0.75)	4.5 (0.56)	3.05 (0.55)	0.29
5	19 (16.4)	2.21 (0.43)	2.09 (0.47)	3.0 (0.51)	0.38
6	31 (26.7)	2.04 (0.56)	1.9 (0.47)	1.57 (0.34)	0.33

T1=time 1; T2=time 2; T3= time 3; HC= Homogeneity coefficient

Cluster 1: Initially high levels of burnout, followed by recovery to moderate level

This cluster displayed initially high levels of burnout at T1, followed by declining to moderate levels of burnout. The development of burnout was reflected in concurrent changes of job strain and depression scores. The development of sleep problems did not follow this pattern as these levels were slightly higher and more stable. The results of the χ^2 -analyses showed that the women in this cluster were also characterized by the personality characteristics of high stress susceptibility and high anxiety (Table 12).

Cluster 2: Burnout levels developing from moderately low to high levels and recovering

The development of burnout levels over time in this cluster was reflected in concurrent changes in sleep problems and depression scores. The development of job strain did not follow this pattern as these levels were lower and rather stable over time. There were no significant results regarding the χ^2 -tests.

Cluster 3: Initially high and over time increasing levels of burnout

Women in this cluster displayed initially high levels of burnout which were increasing over time and finally reaching the highest mean levels during the second follow-up. This development was reflected in concurrent changes in depression scores as well as in sleep problems. The developmental pattern of job strain was similar to that of burnout, although these levels were lower. The results of the χ^2 -analyses showed that women comprising

this cluster were also characterized by high stress susceptibility and high levels of life stress.

Cluster 4: Initially high and over time slightly increasing levels of burnout, followed by recovery to moderate level.

The development of burnout levels in this cluster was reflected in concurrent changes in depression scores. The development of job strain did not support the pattern of burnout as these levels decreased between T1 and T2. The results of the χ^2 -analyses showed that the women in this cluster were characterized by low sense of coherence, high anxiety and high levels of life stress at baseline.

Cluster 5: Initially low levels of burnout developing to moderate levels

The development of burnout levels in this cluster was reflected in concurrent changes in job strain, depression scores and in sleep problems. The results of the χ^2 -analyses showed that the women in this cluster were also characterized by low stress susceptibility and low anxiety.

Cluster 6: Low and decreasing levels of burnout

Women in this cluster displayed initially low levels of burnout which were decreasing over time and finally reaching the lowest mean levels at T3. The changes of job strain, although significant, did not support the pattern of burnout. The low level of burnout was also reflected in low levels of both depression scores and sleep problems. The results of the χ^2 -analyses showed that women in this cluster were also characterized by high sense of coherence, low stress susceptibility, low anxiety and low levels of life stress.

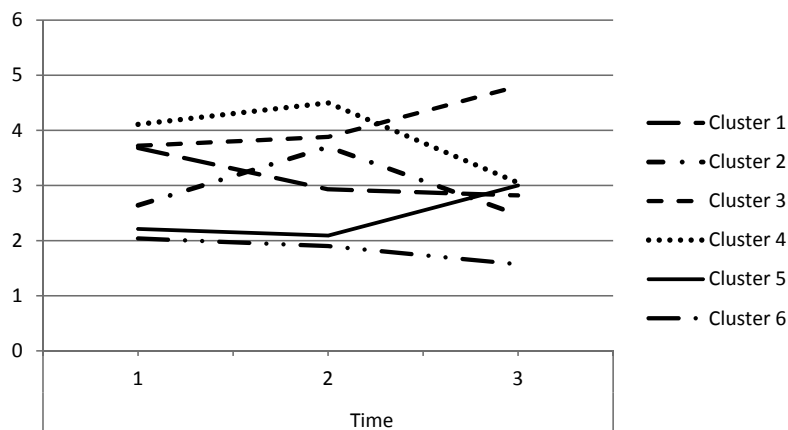
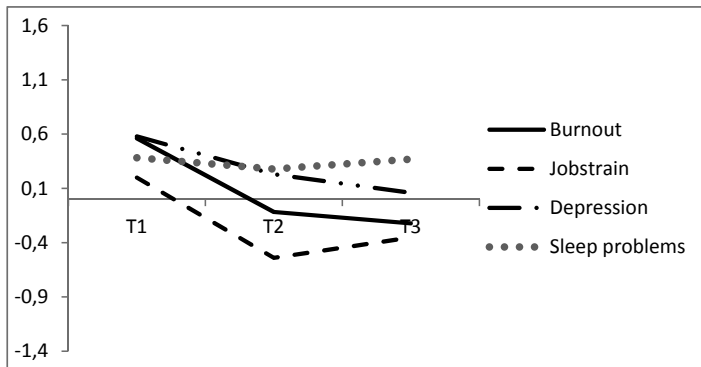
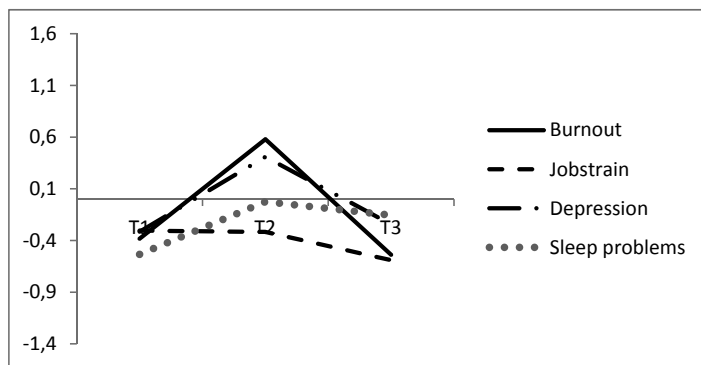


Figure 2. The six clusters graphically plotted

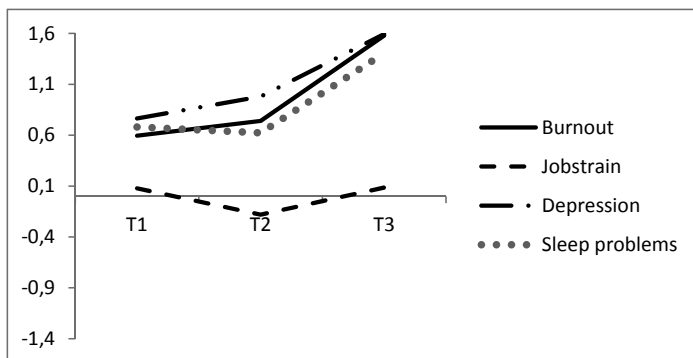
Cluster 1



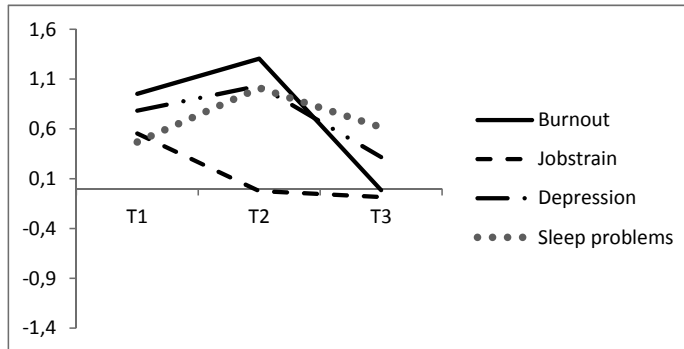
Cluster 2



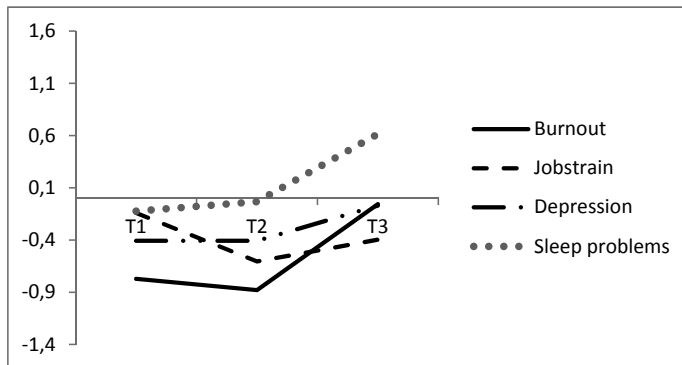
Cluster 3



Cluster 4



Cluster 5



Cluster 6

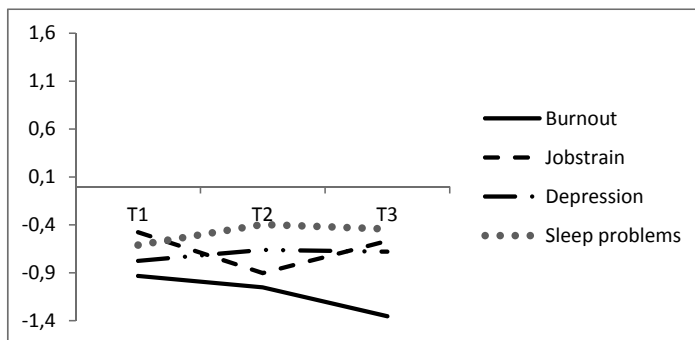


Figure 3. The 6-cluster solution for burnout plotted together with the concurrent development of jobstrain, depression and sleep problems using Z-transformed means at the three time points T1, T2 and T3. One unit on the Y-axis represents one standard deviation. Positive values indicate high levels, negative values low levels.

Table 11. Results of the rANOVAs used to analyze change over time and development among the clusters. Post-hoc tests were used to analyze development over time of the respective variable in the different clusters.

		Across all 3 waves			Between T1 and T2			Between T2 and T3		
	Cluster	F	p	η^2	F	p	η^2	F	p	η^2
Burnout (Time)		1.83	0.167	0.02	0.18	0.675	0.002	2.79	0.098	0.02
Burnout (Cluster x Time)		22.60	0.001	0.51	12.59	<0.001	0.36	33.27	<0.001	0.60
Post-hoc (Time)		17.83	0.001	0.50	22.70	0.001	0.56	0.85	0.370	0.05
	1	40.11	0.001	0.74	47.38	0.001	0.77	58.56	0.001	0.81
	2	7.66	0.002	0.32	0.29	0.596	0.02	10.39	0.005	0.39
	3	30.22	0.001	0.68	4.11	0.062	0.23	53.53	0.001	0.79
	4	26.44	0.001	0.60	1.29	0.270	0.07	40.57	0.001	0.69
	5	13.28	0.001	0.31	3.26	0.081	0.10	13.32	0.001	0.31
	6									
Control (Cluster x Time)		2.66	0.010	0.12	3.30	0.009	0.15	1.12	0.354	0.06
Post-hoc (Time)		6.81	0.010	0.30	8.15	0.011	0.34	0.02	0.884	0.00
	1	0.98	0.360	0.08	0.51	0.490	0.04	5.58	0.036	0.32
	2	0.02	0.927	0.00	0.04	0.840	0.00	0.06	0.804	0.00
	3	9.26	0.001	0.44	16.19	0.002	0.57	0.06	0.811	0.00
	4	0.38	0.591	0.02	0.47	0.505	0.03	0.21	0.657	0.01
	5	1.28	0.286	0.05	0.57	0.457	0.02	0.82	0.375	0.003
	6									
Jobstrain (Cluster x Time)		1.94	0.062	0.09	2.99	0.015	0.14	1.77	0.127	0.09
Post-hoc (Time)		10.43	0.001	0.40	19.73	<0.001	0.55	1.69	0.212	0.09
	1	2.33	0.129	0.16	0.01	0.907	0.001	5.39	0.039	0.31
	2	0.52	0.497	0.039	3.39	0.089	0.21	0.81	0.385	0.06
	3	3.38	0.081	0.22	5.75	0.034	0.32	0.20	0.660	0.02
	4	6.85	0.005	0.30	12.06	0.003	0.43	4.26	0.056	0.21
	5	13.59	<0.001	0.34	24.07	<0.001	0.48	13.55	0.001	0.34
	6									

	Cluster	F	p	η^2	F	p	η^2	F	p	η^2
Sleep problems (Cluster x Time)										
Post-hoc (Time)										
	1	2.54	0.008	0.10	2.02	0.082	0.08	3.81	0.003	0.15
	2	0.11	0.890	0.01	0.19	0.669	0.01	0.13	0.719	0.01
	3	3.11	0.061	0.18	6.02	0.028	0.30	0.34	0.567	0.02
	4	6.23	0.010	0.28	0.09	0.774	0.01	12.23	0.003	0.43
	5	1.69	0.205	0.11	3.93	0.067	0.22	1.74	0.209	0.11
	6	4.90	0.027	0.21	0.39	0.539	0.02	4.87	0.041	0.21
		2.16	0.134	0.07	6.82	0.014	0.19	0.17	0.687	0.01
Depression (Cluster x Time)										
Post-hoc (Time)										
	1	5.05	<0.001	0.19	3.34	0.008	0.13	5.58	<0.001	0.20
	2	5.42	0.009	0.23	4.50	0.048	0.20	1.28	0.273	0.07
	3	8.56	0.004	0.38	12.81	0.003	0.48	7.81	0.014	0.36
	4	4.01	0.043	0.20	1.14	0.301	0.07	2.83	0.112	0.15
	5	3.12	0.062	0.18	0.86	0.369	0.06	5.18	0.039	0.27
	6	2.25	0.140	0.11	0.00	1.00	0.00	10.41	0.005	0.37
		0.80	0.454	0.03	1.51	0.229	0.05	0.04	0.845	0.00
Life stress (Cluster x time)										
	1	2.33	0.015	0.10	2.79	0.021	0.11	2.63	0.028	0.11
	2	0.50	0.584	0.03	0.11	0.741	0.01	0.75	0.399	0.04
	3	3.01	0.081	0.18	6.14	0.027	0.31	0.35	0.570	0.02
	4	5.89	0.007	0.28	3.74	0.072	0.20	11.02	0.005	0.42
	5	0.13	0.857	0.01	0.21	0.652	0.02	0.01	0.945	0.00
	6	0.07	0.930	0.00	0.03	0.870	0.00	0.15	0.699	0.01
		0.29	0.737	0.01	0.59	0.450	0.02	0.27	0.608	0.01

Table 12. Characterization of the clusters using χ^2 - tests. Bold numbers indicate significance.

Variable		Clusters %							χ^2	<i>p</i>
		Total	1	2	3	4	5	6		
Socioeconomic status	High	68.1	73.7	66.7	76.5	66.7	47.4	74.2	5.14	0.399
SSP Stress susceptibility	High	47.4	78.9	40.0	87.5	93.3	31.6	16.7	42.95	0.001
SSP Psychic trait anxiety	High	54.4	68.4	46.7	56.3	86.7	15.8	23.3	27.73	0.001
Sense of coherence (T2)	Low	48.7	57.9	46.7	68.8	93.3	36.8	19.4	26.96	0.001
Sense of coherence (T3)	Low	50.4	57.9	40.0	68.8	80.0	59.9	22.6	18.51	0.002
Depression scores (T1)	High	28.7	57.9	13.3	52.9	53.3	5.3	6.7	31.2	0.001
Depression scores (T2)	High	33.9	42.1	46.7	64.7	80.0	5.3	0.0	45.42	0.001
Depression scores (T3)	High	31.3	36.8	13.3	88.2	46.7	21.1	3.3	41.64	0.001

T1=time 1; T2=time 2; T3= time 3

DISCUSSION

The overall aim of the present thesis was to study psychological and physiological aspects of stress in middle-aged women focusing on the associations between adverse psychosocial work environment and the physiological stress responses. A second aim was to study individual differences in a longitudinal perspective by identifying a number of distinct developmental patterns of burnout among the women over a nine year period.

In the following the findings of the empirical studies are discussed separately.

Study I

The results of study 1 showed that high cortisol levels were significantly associated with high demands at work in middle-aged women. This finding is supported by previous research. For example, Kunz-Ebrecht, Kirschbaum and Steptoe (Kunz-Ebrecht, Kirschbaum, & Steptoe, 2004) found in a recent study of work stress that cortisol awakening responses were positively associated with high job demands. When sustained over a prolonged period, this relationship may predispose towards negative health outcomes. Earlier findings have indeed shown that job strain is associated with a higher incidence of CHD (Kuper & Marmot, 2003; Schnall, Landsbergis, & Baker, 1994) and sickness absence (Vahtera, Kivimäki, Pentti, & Theorell, 2000). Two recent studies also indicated that increasing demands and job strain were related to increasing health problems for women (Krantz & Östergren, 2001; Muhonen & Torkelson, 2003).

It is noteworthy that more than two thirds of the women both at baseline and on follow-up reported having a stressful working situation in response to an interview item. The women listed the following demands as stressors: time pressure, attending to several things at the same time and too great responsibility/ too high demands. Similar findings were reported by Swedish statistics on the work environment (*The Work Environment Survey 2003*, 2003): 58% of the women felt that they had too high a workload. The study also reported that there had been no change in the work situation for women since 2001.

The present study also showed that women with low social support from their coworkers had higher cortisol levels at baseline. This result provides additional evidence for the direct effect model of social support, which postulates that social support reduces the level of strain. A few recent studies have, in fact, demonstrated an inverse relationship between cortisol and social support (Heinrichs, Baumgartner, & Kirschbaum, 2003; Rosal, King, Ma, & Reed, 2004; Schnorpfeil et al., 2003).

It is interesting to note that the women had significantly lower cortisol levels, as well as lower job strain scores, on follow-up. It is possible that the psychological interview focusing on various aspects of the women's lives may have served as an intervention. The women may have become more aware of their stress and learned to cope with it as a consequence of reflecting on their lives. Thus, the interview may have functioned as a

trigger for change. Furthermore, menopausal transition itself is characterized by psychological development and change, offering an opportunity for reflection and personal growth (Busch, Barth-Olofsson, Rosenhagen, & Collins, 2003). Also, the fact that the women whose lipid values exceeded the normal range, received feedback on their lipid profiles may have increased their awareness and their willingness to make life style changes in the direction of adopting healthier dietary habits and of reducing work stress. In the follow-up interview, a number of the women spontaneously stated that they had made such life changes.

WHR predicted high cortisol levels on follow-up. Both WHR and BMI had an inverse relationship with cortisol. Earlier studies have shown inconsistent results concerning these associations. Ukkola et al. (2001) (Ukkola et al., 2001) reported a negative correlation between cortisol and BMI in both men and women, whereas Steptoe, Kunz-Ebrecht, Brydon and Wardle (2004) (Steptoe, Kunz-Ebrecht, Brydon, & Wardle, 2004) found no significant associations for either men or women. The same study also reported a positive correlation between WHR and cortisol response to awakening in middle-aged men but not in middle-aged women.

Contrary to expectations, the women had significantly lower WHR in the follow-up. Earlier studies have reported an increase in BMI, WHR and abdominal fat distribution following menopause (Berg, et al., 2004). The contrary effect in the present study may reflect the feedback the participants received about their lipid profiles, and the pedagogic nature of the dietary questionnaire used in the study. The women may have adopted healthier dietary habits which may have been reflected in the trend ($p=0.056$) toward ingesting less fat on follow-up.

In this study there were no associations between menopausal status on cortisol levels. However, the use of HRT was a significant predictor of cortisol levels on follow-up, and was nearly significant at baseline; thus, both baseline and follow-up show the same trend. Therefore, this study suggests that HRT may exert a stimulatory effect on the pituitary and the adrenal cortex. However, the mechanism behind this association is still unknown and conflicting results have been reported: Lobo et al. (1982) (Lobo, Goebelsmann, Brenner, & Mishell, 1982) and Fonseca et al. (2001) (Fonseca, Basurto, Velazquez, & Zarate, 2001) showed a significant association between high cortisol levels and HRT use, whereas other studies have shown a positive association with low cortisol levels (Bernardi et al., 2003).

Conclusions

Study I showed that work-related demands and lack of social support were associated with high cortisol levels in middle-aged women. High demands and low social support predicted high cortisol levels at baseline, but not on follow-up. Furthermore, the mean levels of cortisol were lower on follow-up and the women also rated less job strain. The results of this study were in general agreement with major trends reported in the literature relating psychosocial aspects of working life to stress, with cortisol values serving as a viable proxy for overall stress levels. This is important as little direct evidence had been

available for women in this age group. Thus, the women in transition to menopause, despite some variation across the group and over time, showed a rather consistent relationship between work-related stress and cortisol levels.

Study II

This study showed a significant association between psychosocial work environment and lipid levels in perimenopausal women. Experiencing control at work was significantly associated with higher HDL levels, lower LDL/HDL ratio and total cholesterol/HDL ratio in the multivariate analyses. These results are in agreement with earlier findings that showed an adverse lipid profile in middle-aged women with a work situation characterized by low decision latitude (Wamala, Wolk, Schenck-Gustafsson, & Orth-Gomer, 1997). Similar results have been reported for other age groups of men and women as well (Andre-Petersson, Engstrom, Hedblad, Janzon, & Rosvall, 2007; De Bacquer, et al., 2005; Rose, et al., 2006). Low job control has also been associated with a higher risk of cardiovascular disease (Bildt, et al., 2006; Bosma, et al., 1997). Hence, work control appears to have a beneficial effect on lipid levels and therefore, increasing control at work may be a useful intervention for lowering the risk of cardiovascular disease.

Job strain was associated with higher LDL/HDL ratio as well as higher total cholesterol/HDL ratio on follow-up and thus, our study demonstrates that job strain is a significant contributing factor for higher lipid levels in women. Earlier research has shown that there is a strong association between exposure to job strain and CVD for men (Belkic, et al., 2004; Kivimaki, Virtanen, et al., 2006), but the evidence for women is less conclusive (Belkic, et al., 2004; Eaker, Sullivan, Kelly-Hayes, D'Agostino, & Benjamin, 2004; Kobayashi, Hirose, Tada, Tsutsumi, & Kawakami, 2005; S. Lee, Colditz, Berkman, & Kawachi, 2002). There are several explanations for this: first of all, studies of women are few, and consequently drawing conclusions from limited available data is problematic. Secondly, some studies (Kobayashi, et al., 2005; S. Lee, et al., 2002) have investigated women in only a single occupation or a single workplace and therefore, due to the insufficient variability of demands in different occupations, the demand-control model may not have detected the effects of job strain.

It is interesting to note that the women reported significantly less job strain on follow-up. In fact, during the interview the women reported an increase in perceived freedom and time for oneself between baseline and follow-up. This could in part explain that ratings of job strain were lower on follow-up. It is possible that the positive perception of their current phase of life translated to the work situation, possibly through more effective coping strategies for work stress.

High work demands were associated with high HDL levels at baseline, a result that is difficult to interpret. Also, earlier studies on the demand aspect have not shown as consistent an association with cardiovascular risk as low decision latitude has (Landsbergis, et al., 2001). We did not observe any significant associations between social

support and lipid levels. Contrary to our findings, several other studies have shown that low levels of social support are associated with an increased risk of CHD and myocardial infarction for both men and women (Andre-Petersson, et al., 2007; De Bacquer, et al., 2005; Hammar, et al., 1998; Hemingway, Malik, & Marmot, 2001). Furthermore, social support has been shown to predict psychological well-being in a recent study of cardiovascular risk factors among blue- and white-collar male workers (Rose, et al., 2006).

Controversy still exists as to whether natural menopause is an independent risk factor for cardiovascular disease, or whether the adverse changes in lipoproteins are associated with other factors such as age, decrease in estradiol levels, change in intra-abdominal fat or in lifestyle, such as diet or exercise. In the present study age turned out to be a significant predictor of higher total cholesterol levels in line with earlier research that has reported age-related changes of lipoprotein levels in middle-aged women (Berg, et al., 2004; G. Hall, et al., 2002; Schubert et al., 2006). However, our data do not permit us to draw conclusions as to the role of menopause since only a small proportion of the women had become postmenopausal during the study. In the univariate analyses this group of women had higher total cholesterol levels as measured on follow-up, a result that is supported by earlier studies (Berg, et al., 2004; Carr, et al., 2000; Fukami, et al., 1995; Kuh, et al., 2005).

HRT use was a significant predictor of lower cholesterol levels in the multivariate analyses. Beneficial effects of HRT use on lipid profiles in postmenopausal women have been reported in several observational studies (Man et al., 2001; Mattiasson, Rendell, Tornquist, Jeppsson, & Hulthen, 2002; Roussel et al., 2002), however, the positive effects of HRT on lipoprotein levels were challenged by the results from the Women's Health Initiative study, which showed no benefit and possibly an increased risk of CHD (Manson et al., 2003). More recently, a more balanced view of these results has emerged after reanalysis of the data indicating that there may be benefits of HRT on CVD risk, particularly if the treatment is initiated close to menopause. However, HRT is not generally recommended for prevention of CVD (Rossouw et al., 2007). A recent paper suggests that timing, duration of therapy and other health risks of the women are important considerations. The "window of opportunity" regarding HRT refers to initiating treatment around the age of menopause; in the early 50's rather than later (Maclaran & Stevenson, 2012). Thus, many unresolved issues remain concerning treatment regimens, dose of estrogens, as well as mode and timing of administration (Sandset, 2006).

Women with a higher socioeconomic status (SES) had more favourable LDL/HDL ratios and total cholesterol/HDL ratios than women with lower SES. The women with high SES reported having more control over their work situation and less job strain. They also consumed less fat and had lower systolic blood pressure than women with lower SES. These results are in agreement with earlier studies showing that lower SES is associated with an adverse lipid profile and an increased risk of cardiovascular events (Albert, Glynn, Buring, & Ridker, 2006; Ljung & Hallqvist, 2006; Wamala, et al., 1997). The mechanism underlying the relationship between low SES and CVD remains uncertain. Proposed

pathways for this relationship are only partly explained by lifestyle. In addition other factors, such as access to care, chronic psychosocial stress, social support and job control have been suggested as possible confounding factors (Albert, et al., 2006; Muennig, Sohler, & Mahato, 2007; Wamala, et al., 1997).

Obesity is a well-known risk factor for CVD (Field et al., 2001; G. Hall, et al., 2002) and in our study high BMI was a significant predictor of lower HDL levels, higher LDL/HDL ratio and higher triglycerides. Also, waist circumference and WHR have been suggested as being critical measures of intra-abdominal fat predicting CVD risk factors (Dalton et al., 2003; Ho et al., 2001). In the present study WHR was significantly associated with an atherogenic lipid profile both at baseline and on follow-up. Previous studies have shown that the transition from premenopause to postmenopause is associated with adverse changes in abdominal fat deposition (Chang et al., 2000; Donato, Fuchs, Oppermann, Bastos, & Spritzer, 2006). This result was replicated in our study as the small group of women who transitioned to menopause had higher BMI. However, we found no significant differences in either BMI or WHR between the different menopausal groups. Furthermore, we did not observe any significant changes of BMI and WHR between the baseline and follow-up during this relatively short interval.

As reported in study I, the women seemed to have made some changes toward a healthier life style as fewer women were smokers on follow-up and fewer were physically inactive. Thus, the study may, have served as an intervention since the women whose lipid profiles exceeded the recommended limits received feedback on their lipid values, and thus it may have increased their motivation to make life style changes. Interestingly, alcohol consumption did not follow this pattern since the consumption was found to be higher on follow-up. This change may be viewed as being in line with the general increase in women's alcohol consumption since the mid- 90s in Sweden (*Gränslös utmaning - alkoholpolitik i ny tid. Limitless challenge - alcoholpolitic in modern time*, 2005).

Moderate to high alcohol consumption was significantly associated with higher HDL levels and with lower LDL/HDL ratios. Other studies have reported a beneficial effect of moderate alcohol intake on HDL levels among middle-aged women (Sillanaukee, Koivula, Jokela, Pitkajarvi, & Seppa, 2000) and in postmenopausal women (Baer et al., 2002; Sierksma et al., 2004). However, it should be recognized that as there is no general consensus as to the definition of moderate drinking, the reference categories vary across different studies, which makes it difficult to compare results. Also other biases are often present such as variations in alcohol intake over time and the tendency to underestimate one's alcohol consumption (Seppa, Lof, Sinclair, & Sillanaukee, 1994).

The role of HDL as a major predictor of CVD among women is not well established and instead, alternative measurements have been suggested, such as the ratios of total cholesterol/HDL and LDL/HDL as they concurrently account for both atherogenic and protective lipid fractions (Natarajan et al., 2003; Ridker, Rifai, Cook, Bradwin, & Buring, 2005; Shai, et al., 2004). To our knowledge there is considerable paucity of studies on the

associations between these ratios and work stress. Thus, the present study lends support to the predictive utility of the lipid ratio metrics.

Conclusions

Study II demonstrated an association between the psychosocial work environment and lipid levels as a mediating pathway for women's cardiovascular health at menopause. Job strain predicted an adverse lipid profile, whereas work control predicted a favourable profile. As for life style variables smoking, a high BMI and WHR predicted an unfavorable lipid profile. Interestingly, age but not menopausal status was associated with lipid levels at baseline and on follow-up. HRT use was a significant predictor of lower cholesterol levels in the multivariate analyses. Higher SES was associated with positive change in HDL cholesterol levels, whereas lower SES was associated with a negative change over time.

Study III

The aims of the third study were to identify developmental patterns of burnout in middle-aged women and to evaluate whether work-related and individual factors are associated with concurrent changes in burnout. For this purpose, a person-oriented approach was adopted in order to explore the occurrence of homogenous classes of individuals characterized by similar levels of burnout. When using a variable-based approach the results showed no significant changes in burnout levels over time. This reflects the fact that the group mean levels were rather stable across time. However, when applying an individual-oriented approach different developmental pathways were identified as six clusters of burnout were disclosed.

Three clusters (1, 3 and 4) were of particular interest because they presented elevated burnout levels at the initial evaluation and also because they differentiated across time. Clusters 1 and 4 showed moderate burnout levels. The burnout levels in cluster 3 reached the highest levels in this study. It is important to point out that 26% of the women progressed through the course of the study with little or no salient deterioration in their burnout profiles. The largest cluster (6), in fact, showed the consistently lowest burnout levels. The burnout levels in cluster 5 were also low at baseline, however increasing to moderate levels over the nine year period.

The burnout levels in clusters 1, 3 and 4 were elevated at baseline. Clusters 1 and 4 were similar to the extent that these burnout levels decreased whereas those of cluster 3 increased throughout the study. Women in cluster 4 reported a significant degree of life stress. As for cluster 3, life stress increased significantly between the first and the second follow-up indicating that stress in the lives of these women increased and this may be an important antecedent of the increase in their burnout levels. Besides the measure of life stress used in this study the women reported sources of life stress such as concern for ailing parents, for their own health or that of their partner in the interviews. Women in

these three clusters were also more sensitive to stress since their stress susceptibility and their state anxiety was high. Conversely, the burnout levels in clusters 5 and 6 were low and these women showed low levels of life stress, low levels of stress susceptibility and anxiety as well as high levels of sense of coherence. Taken together, our results suggest that life stress combined with work stress may play an important role in explaining burnout in middle-aged women. It should be emphasized that this longitudinal study followed the women over a considerable segment, nine years, of their working lives. This period of life for women, that is midlife, is associated with a range of life events and transitions which can be stressful and challenging for many women (Busch, et al., 2003). Furthermore, other studies have shown that emotional strain outside the work environment may contribute to burnout since family-related factors and adverse life situations, such as strained economy or low social integration have been associated with burnout (Bekker, Croon, & Bressers, 2005; Burisch, 2002; Norlund, et al., 2010).

Previous research has found that high demands and low control were associated with high burnout levels in women (Demerouti, Bakker, Nachreiner, & Schaufeli, 2000; Lindblom, Linton, Fedeli, & Bryngelsson, 2006; Magnusson Hanson, Theorell, Oxenstierna, Hyde, & Westerlund, 2008; Norlund, et al., 2010; Rafferty, Friend, & Landsbergis, 2001; Schaufeli & Bakker, 2004). In addition, high job strain was also found to be associated with high burnout levels (Grossi, et al., 2003). In the present study we found partial support for this notion. In cluster 1 job strain reflected a similar pattern to that of burnout as both job strain and burnout levels decreased significantly between the baseline and the first follow-up. However, in cluster 4, even though the development of job strain was significant, the overall pattern did not follow that of burnout which increased between baseline and the first follow-up. This could be due to the fact that work control which is included in the job strain measure increased significantly between the baseline and the first follow-up in this cluster. Thus, it is possible that decreased control is associated with increasing levels of burnout for these women. In the present study no significant associations between **social support** and burnout were found. However, the χ^2 -analyses revealed a trend: women with high levels of burnout received low degree of support and correspondingly, women with low levels of burnout reported high degree of support. Accordingly, earlier studies have clearly linked lack of social support to burnout (Kalimo, et al., 2003; R. T. Lee & Ashforth, 1996; Schaufeli & Enzmann, 1998).

Sleep problems and depression are considered to be associated with burnout. In our study the development of burnout from lower to higher levels over time was reflected in concurrent changes in increasing **sleep problems** in three out of six clusters (2, 3 and 5). The women in cluster 6 with low burnout levels displayed low levels of sleep disturbances. These results are supported by earlier research that has demonstrated an association between burnout and self-reported sleep problems (Grossi, et al., 2003; Melamed, et al., 2006; Peterson, et al., 2008; Tokuda, et al., 2009). This relationship has also been validated with a physiological measurement of sleep by using polysomnographic recording (Ekstedt, et al., 2006; Soderstrom, et al., 2004). A recent longitudinal study in the general working population showed that high work demands increased the risk of

developing insomnia (Jansson-Frojmark, Lundqvist, Lundqvist, & Linton, 2007). It has also been suggested that burnout and sleep problems may recursively predict each other's development and intensity over time (Armon, Shirom, Shapira, & Melamed, 2008). Thus, these results indicate that impaired sleep may influence the development of fatigue or exhaustion and thereby predispose one to burnout. On the other hand, burnout seems to affect sleep and thereby increase fatigue.

The results showed that the development of burnout levels was reflected in concurrent changes in **depression** scores in five clusters but not in cluster 6 which displayed low levels of burnout. Previous research has demonstrated that burnout and depression are strongly related, share common variance and may share common antecedents (Ahola, et al., 2005; Glass & Mcknight, 1996; Iacovides, Fountoulakis, Kaprinis, & Kaprinis, 2003; Schaufeli & Enzmann, 1998). Thus, a question of a conceptual overlap between the constructs has been raised in the literature. One possible explanation for the partial overlap is that burnout mediates the association between psychosocial work characteristics and depression. Hence, it has been suggested that job strain predisposes individuals to depression through burnout and to burnout either directly or through depression (Ahola & Hakanen, 2007; Ahola et al., 2006).

An interesting finding of the present study was the fact that there were individual differences in **stress susceptibility, levels of anxiety and sense of coherence**. Women with moderate to high levels of burnout displayed high stress susceptibility and high anxiety (clusters 1, 3 and 4). Conversely, women with low levels of burnout displayed low stress susceptibility and low anxiety (clusters 5 and 6). Individuals with high scores of psychic trait anxiety are described as worried and lacking in self-confidence and individuals with high scores in stress susceptibility are characterized as easily fatigued and feeling uneasy when urged to hurry (Gustavsson, et al., 2000). To the best of our knowledge the relationship between burnout and personality has not been addressed earlier using the Swedish Scales of Personality (Hallman, et al.), rather other measures, such as the Five Factor Model, have been used to analyze this relationship. Previous research has reported an association between burnout and the personality factor of neuroticism (Hochwälder, 2006; Swider & Zimmerman, 2010). Furthermore, burnout has been associated with low emotional stability, high levels of anxiety and low self-esteem (Alarcon, Eschleman, & Bowling, 2009; Gustafsson, Persson, Eriksson, Norberg, & Strandberg, 2009; Peterson, et al., 2008). Thus, these results indicate that individual-level predictors, such as personality do play an important role in the development of burnout.

In this study women who had moderate to high levels of burnout displayed a low sense of coherence (clusters 1, 3 and 4) and conversely, women who had low levels of burnout displayed a high sense of coherence (cluster 6). These results are in line with earlier studies that have demonstrated that strong SOC is a health promoting resource (see a review: Eriksson & Lindström, (Eriksson & Lindstrom, 2006)). Strong SOC has also been related to better quality of life (Eriksson & Lindstrom, 2007). The predictive power of SOC has been less studied, however there is evidence showing that SOC can be a long-term predictor of burnout as it has been reported that SOC had weakened in a group with

serious burnout during a 10-year follow-up. On the other hand, SOC had developed in a positive direction in individuals without burnout (Kalimo, et al., 2003). Hence, these results indicate that individual resources such as SOC seem to exercise a protective influence on health and thus decrease vulnerability to burnout.

Conclusions

In contrast to previous research suggesting that burnout is a stable construct over time, the present study identified distinct subgroups of women showing different developmental patterns of burnout during a nine-year period. Furthermore, our findings showed that the development of burnout was accompanied by concurrent changes in life stress, sleep problems, depression as well as work-related and individual factors.

Strengths and limitations

This thesis addressed stress reactivity in women at midlife with particular attention to stress indices of working life in relation to cardiovascular health and the development of burnout in middle-aged women. This age group of women is interesting to study partly because this period of life entails both biological and psychological changes. One of the issues still debated is whether the female sex hormones do play a protective roll in the development of cardiovascular disease or not. Another interesting issue concerning this age group is that it is middle-aged women who are long-term sick listed the most. Furthermore, as results concerning the association between work stress and both cortisol and lipid levels in women are still contradictory and more studies including women are still needed, this thesis has aimed at contributing to this issue. Moreover, in this thesis the subjective measures of stress have been combined with objective measures in the form of biological stress markers.

An additional strength of this thesis is that the data derives from a longitudinal study over a time period of nine years. As longitudinal studies are still relatively rare this thesis has provided some additional evidence on the relationships between work stress on one hand and cortisol and lipid levels on the other. This thesis has also investigated the development of burnout over time and identified distinct sub-groups of women displaying different developmental patterns of burnout. This finding is interesting as it stands in contrast to previous research that has regarded burnout as a stable construct over time.

There are however, also a few limitations worth mentioning.

It is important to note that the use of questionnaires in this thesis rely on subjective appraisals. Self-reports are affected by perceptual biases as our perception is affected by moods, attitudes and by cognitive processes, social desirability etc (Podsakoff, MacKenzie, Lee, & Podsakoff, 2003) Thus, the results of this thesis are vulnerable to self-report bias and reporting bias (common method bias) is a potential source of type I error (false positive findings). Although both objective work characteristics as well as the

subjective perception of them may affect health, it is recommended to use both subjective and objective measures.

One limitation of *study I* was that a single measure of cortisol was used. Although it would have been desirable to collect several blood samples in the morning, it would not have been practical to obtain these from the relatively large sample of participants given their busy schedules as working women. Sampling of saliva however, would have been a more cost-effective alternative. To date, intra-person stability from day to day of plasma cortisol levels has not been investigated extensively. However, two studies have demonstrated stability in plasma concentrations in women (Huizenga et al., 1998; Kirschbaum, et al., 1992). Another limitation of this study was that the exact time of awakening was not controlled for and thus this may have affected some of the cortisol values since the peak level usually occurs 30 min after awakening (J. C. Pruessner, et al., 1997).

A limitation of *study II* was that the time interval between baseline and follow-up was relatively short in order to detect changes in lipid levels related to menopausal status and age. In addition, only a small group of women had become postmenopausal during the study and thus it was not possible to draw conclusions of the role of menopause.

In *study III* the dropout rate of the women between the first and the second follow-up was 13 % and the reason for a number of these women declining to participate may have been that they were sick-listed for burnout. Thus, these dropouts may have influenced the results to some extent. Another limitation was that the measure of life stress used in this study was not optimal as it combined both work and private stress. Furthermore, since the sample had an overrepresentation of women from the high income group this may have implications for the generalizability as the clusters merged in this study may not represent typical burnout trajectories for all working middle-aged women.

Future considerations

Our understanding of the association between the psychosocial work environment and health has increased significantly over the last half a century. The following adverse characteristics of a work situation are considered to be risk factors for stress and ill health: high psychological demands, lack of control of the work situation, and lack of social support (Belkic, et al., 2004; Kivimaki, Virtanen, et al., 2006; Williams, 2008). However, it is important to emphasize that these adverse work situations become a risk for ill health when one or more of the following factors are also present: long duration, high frequency and insufficient possibilities for recovery. Thus, it can be concluded that the experience of stress is a matter of balance or rather, lack of balance between these factors. As to etiology, mainly two central pathways between exposure to adverse work situation and health outcomes have been distinguished: a psychophysiological mechanism and a behavioral lifestyle mechanism (Geurts & Sonnentag, 2006; Siegrist & Rödel, 2006).

Job strain is the most widely used dimension of work stress in studies of the relation between work stress and cardiovascular risk. This association has been observed both among men and women, however, a recent review (Belkic, et al., 2004) states that the evidence of an association between exposure to job strain and CVD was strong and consistent for men whereas for women this association was less conclusive. There are several explanations for this: *first of all*, studies of women have been too few and, consequently, drawing conclusions from limited available data is problematic.

Second, traditional diagnostic strategies may have failed to identify women at risk as women may display other symptoms than the typical cardiac symptoms of chest pain that have primarily been based on the experience of white middle-aged men. Thus, as accurate descriptions of women's typical symptoms have been lacking, this may have led to inaccurate diagnosis of women and consequently affected the results of many studies (Douglas & Ginsburg, 1996; McSweeney et al., 2003).

Third, many studies do not take estrogen status or the use of hormone replacement therapy (HRT) into account. Premenopausal women have a lower risk of CVD compared to age-matched men and as this gender advantage for women disappears gradually after menopause, it is suggested that estrogen plays a cardioprotective role in women (Yang & Reckelhoff, 2011). It is however still unclear whether HRT has beneficial or detrimental effects on cardiovascular risk as both have been reported (Manson, et al., 2003; Rosano, Vitale, & Fini, 2009). Thus it is plausible that a lack of adjustment for hormone-related risk among women may have weakened the results.

Fourth, many studies have not taken the combination of work and home responsibilities for women into account. A recent Swedish study showed that the traditional gender pattern concerning the division of household responsibilities still prevails (Berntsson, Lundberg, & Krantz, 2006). Women in this particular study reported more symptoms than men and 6.6 more hours/week of total workload (including paid work, household work and childcare) than men. Since women still seem to bear a major burden for home and family responsibilities it is important to acknowledge that the psychological load of the home situation may interact more with the work situation for women in generating illness symptoms than it does among men. Many studies have in fact shown that overload is associated with unexplained symptoms in women (Emslie, Hunt, & Macintyre, 2004; Krantz, Berntsson, & Lundberg, 2005; Lindstrom, 2005). Furthermore, the double exposure to stress from both work and family was associated with the highest risk for CVD in women (Orth-Gomer & Leineweber, 2005; Wang et al., 2007). Thus, it is essential to include a more complete assessment of the stress in home environment in studies of work and health among women.

Another important issue to mention is that measuring long-term work stress with a single-time exposure may underestimate the effect of stress as a CHD risk factor since CHD develops over a long time period. Also, if stress levels are changing over time a single time measure may not provide an accurate estimate of long-term stress. Thus, it is advisable to include multiple measurements of work stress over time as this would

subsequently improve the estimation of long-term exposure and therefore reduce type II error (false negative findings). Also, large-scale epidemiological cohorts are referable as they enable subgroup analyses of e.g. different age groups and occupational positions.

The Demand-control model has been widely used in occupational research, however, it has also received some criticism over the years (Kasl, 1996; Kristensen, 1995). De Croon et al. (2000) (De Croon, Van der Beek, Blonk, & Frings-Dresen, 2000) criticized the measure of decision latitude as being too comprehensive and advocated a more precise measure of job control. In their review of studies published during the period 1979-1997 Van der Doef & Maes (1999) (van der Doef & Maes, 1999) found support for the moderating influence of work control and social support to be less consistent for women and conclude that the key factor for these inconsistencies is the conceptualization of demands and control. Thus, they raise the question whether work demands as defined by the model actually applies to all occupational groups. For example, stressors related to interactions with patients and students could constitute an important demand aspect for health care personnel and teachers. In a similar manner, it is reasonable to assume that for example dealing with problems related to different kind equipment is more relevant to certain professions than to others. Hence, it is suggested that the measures of both demands and control should be more sensitive to differences between occupations and thus be defined as more occupation specific.

Personality could be a moderating factor between work stress and the experience of work strain. Certain personality characteristics could be associated with vulnerability whereas others with resistance. Furthermore, they suggest that high control could be more beneficial for certain individuals while low control could suit other individuals. Thus, it is relevant to take into account individual differences and personal characteristics such as stress susceptibility and coping mechanisms.

One of the issues to be solved regarding research on **burnout** is the definition of the concept. Despite of more than three decades of research on burnout the researchers have not been able to agree on a common conceptualization and structure of burnout. One of the main questions is whether burnout should be regarded as a form of extreme fatigue or as a multi-dimensional construct as it is defined by the MBI. It appears that the diverging views are relatively strong as new and improved measures are being developed continuously. The lack of consensus on this matter is also a methodological problem as the different definitions and different ways of measuring burnout reduces the comparability between studies.

Another issue still debated is whether burnout should be conceptualized as a work-related phenomenon or as a phenomenon that is context free? The women in our study stated in the interviews that the causes of burnout were not only work-related but rather that their experience of burnout could be related to challenges in both their private life and work life or in either one of them. These results, however, are still preliminary and have not yet

been published. The fundamental assumption regarding work stress or burnout is that we can measure work stress isolated of life stress in general. This assumption thus implies that we are able to “shut off” our private life as soon as we arrive at work. However, is it not more reasonable to assume that the subjective perception of stress is dependent on the overall perception of stress, whether the source of stress derives from work or from private life?

Thus it seems that the causal processes underlying burnout are not fully understood and consequently it is suggested that combining quantitative studies with qualitative ones would add additional value and thus benefit the research on burnout. For example by using a diary study approach it would be possible to examine situational features as well as individual interpretations and reactions to specific stressors, coping with symptoms and possible lack of resources (Sonnentag, 2005). Furthermore, knowledge on the etiology of burnout as well as identifying early risk factors are pivotal in order to be able to develop more effective means of prevention, treatment and rehabilitation. Especially studies on organizational-level interventions are needed.

Concluding remarks

The overall aim of the present thesis was to study both psychological and physiological aspects of stress in middle-aged women. The main focus was on the associations between adverse psychosocial work environment and the physiological stress responses in terms of cortisol and lipid levels. The findings from this thesis offer further empirical evidence for an association between work-related demands and high cortisol levels in women. Also lack of social support was associated with high cortisol levels. Furthermore, this thesis provides increased support for an association between adverse psychosocial work environment and lipid levels as a mediating pathway for women’s cardiovascular health at menopause as job strain predicted an adverse lipid profile, whereas work control predicted a favourable lipid profile. An additional contribution of this thesis is that it identified distinct subgroups of women showing different developmental patterns of burnout during a nine-year period. This finding stands in contrast to previous research suggesting that burnout is a stable construct over time. Moreover, the thesis showed that the development of burnout was accompanied by concurrent changes in life stress, sleep problems, depression as well as work-related and individual factors.

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